Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1626GMS

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	4	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	5	MAR 02	GBFULL: New full-text patent database on STN
NEWS	6	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	9	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	10	MAR 22	PATDPASPC - New patent database available
NEWS	11	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	12	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	13	APR 04	EMBASE - Database reloaded and enhanced
NEWS	14	APR 18	New CAS Information Use Policies available online
NEWS	15	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS	16	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
NEWS	17	MAY 23	GBFULL enhanced with patent drawing images
NEWS	18	MAY 23	REGISTRY has been enhanced with source information from CHEMCATS
NEWS	19	JUN 06	STN Patent Forums to be held in June 2005
NEWS	20	JUN 06	The Analysis Edition of STN Express with Discover! (Version 8.0 for Windows) now available
NEWS	21	JUN 13	RUSSIAPAT: New full-text patent database on STN
NEWS	22	JUN 13	FRFULL enhanced with patent drawing images
NEWS	23	JUN 20	MEDICONF to be removed from STN

NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that

specific topic.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:38:58 ON 20 JUN 2005

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:39:27 ON 20 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 JUN 2005 HIGHEST RN 852520-85-5
DICTIONARY FILE UPDATES: 19 JUN 2005 HIGHEST RN 852520-85-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

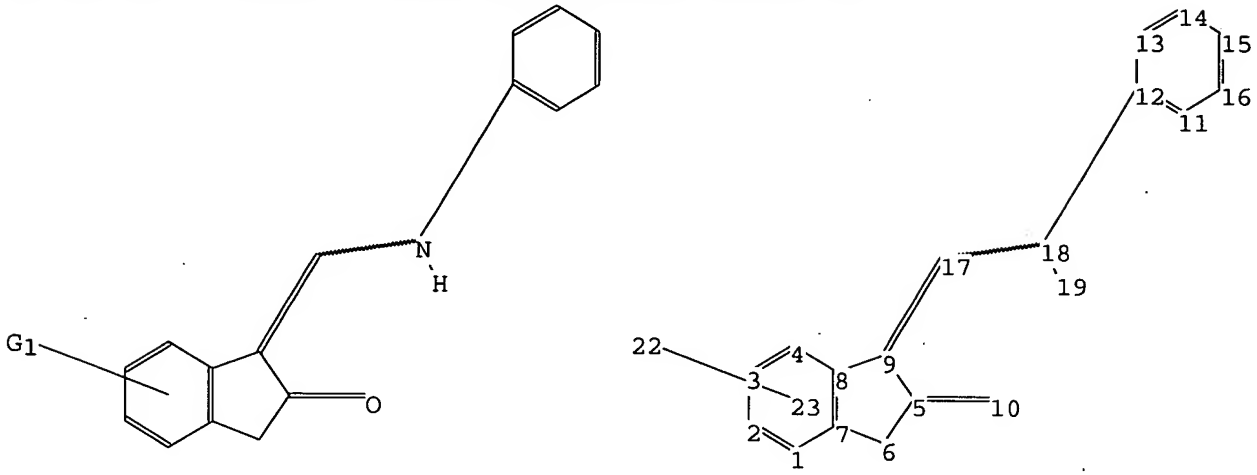
****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more

information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10783325.str



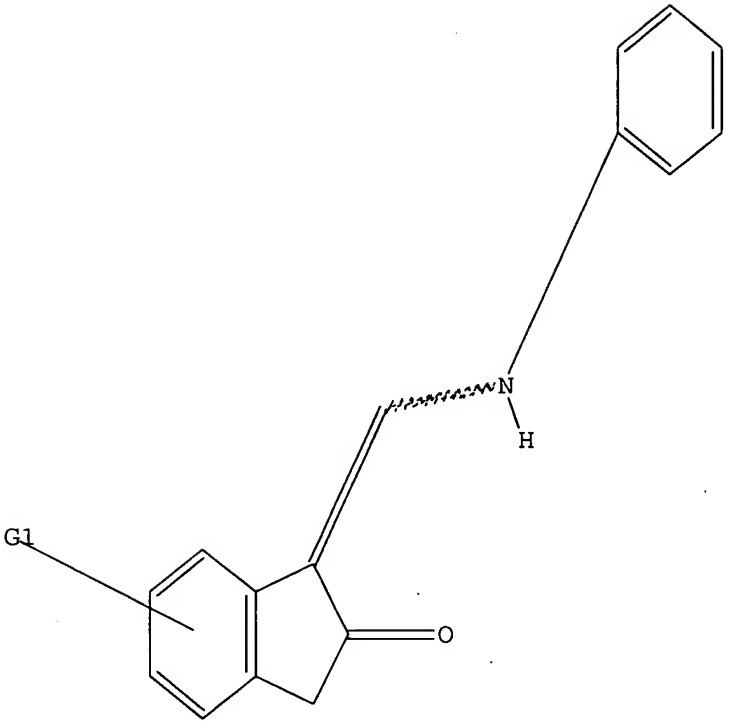
chain nodes :
10 17 18 19 22
ring nodes :
1 2 3 4 5 6 7 8 9 11 12 13 14 15 16
chain bonds :
5-10 9-17 12-18 17-18 18-19
ring bonds :
1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 11-12 11-16 12-13 13-14 14-15
15-16
exact/norm bonds :
5-10 12-18 17-18
exact bonds :
5-6 5-9 6-7 8-9 9-17 18-19
normalized bonds :
1-2 1-7 2-3 3-4 4-8 7-8 11-12 11-16 12-13 13-14 14-15 15-16
isolated ring systems :
containing 1 : 11 :

G1:X,CH3,CN,NO2,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
22:CLASS 23:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 X,Me,CN,NO2,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 11:39:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 119 TO ITERATE

100.0% PROCESSED 119 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1726 TO 3034
PROJECTED ANSWERS: 0 TO 0

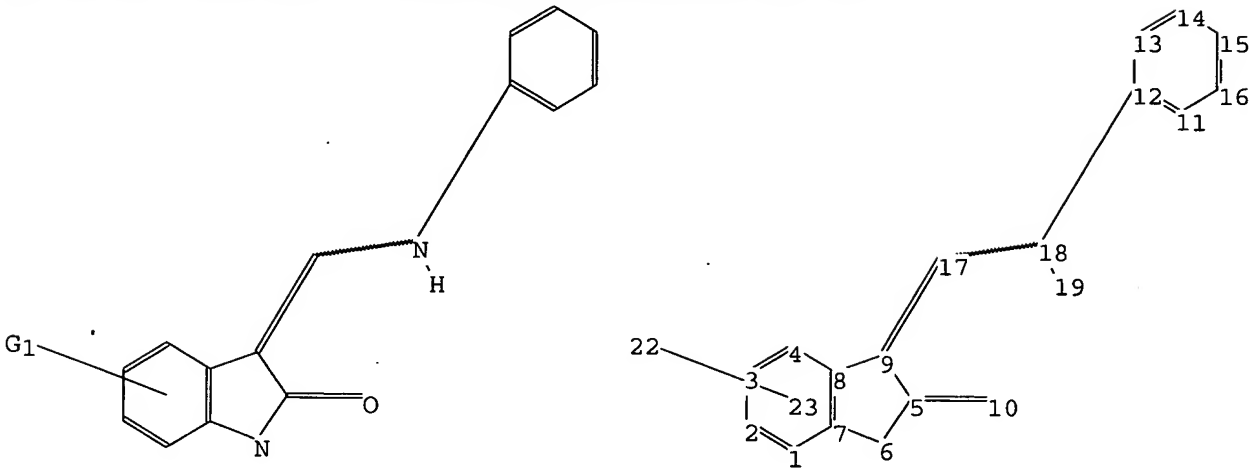
L2 0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 11:39:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2314 TO ITERATE

100.0% PROCESSED 2314 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=>
Uploading C:\Program Files\Stnexp\Queries\10783325a.str



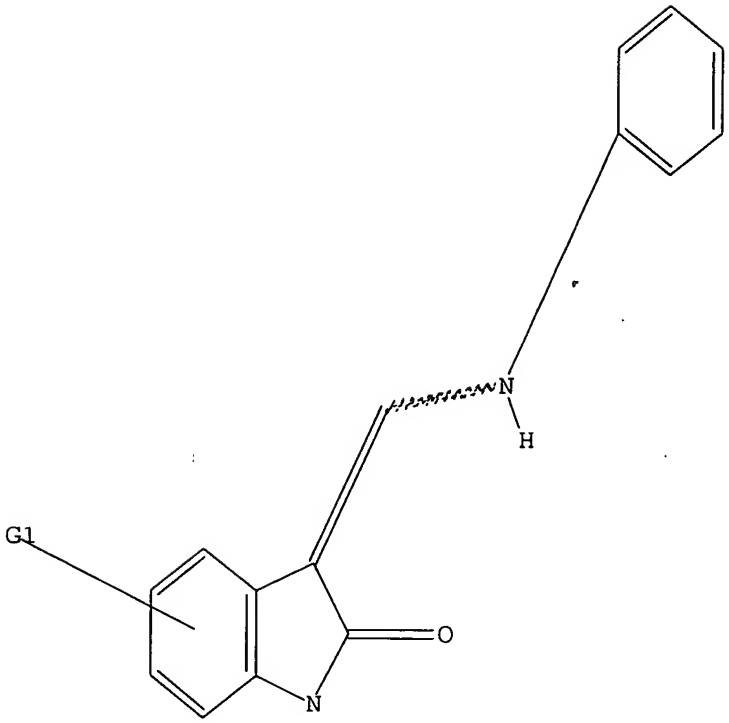
chain nodes :
10 17 18 19 22
ring nodes :
1 2 3 4 5 6 7 8 9 11 12 13 14 15 16
chain bonds :
5-10 9-17 12-18 17-18 18-19
ring bonds :
1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 11-12 11-16 12-13 13-14 14-15
15-16
exact/norm bonds :
5-6 5-10 6-7 12-18 17-18
exact bonds :
5-9 8-9 9-17 18-19
normalized bonds :
1-2 1-7 2-3 3-4 4-8 7-8 11-12 11-16 12-13 13-14 14-15 15-16
isolated ring systems :
containing 1 : 11 :

G1:X,CH3,CN,NO2,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
22:CLASS 23:CLASS

L4 STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4 STR



G1 X,Me,CN,NO2,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l4
SAMPLE SEARCH INITIATED 11:42:07 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 179 TO ITERATE

100.0% PROCESSED 179 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2778 TO 4382
PROJECTED ANSWERS: 1640 TO 2920

L5 50 SEA SSS SAM L4

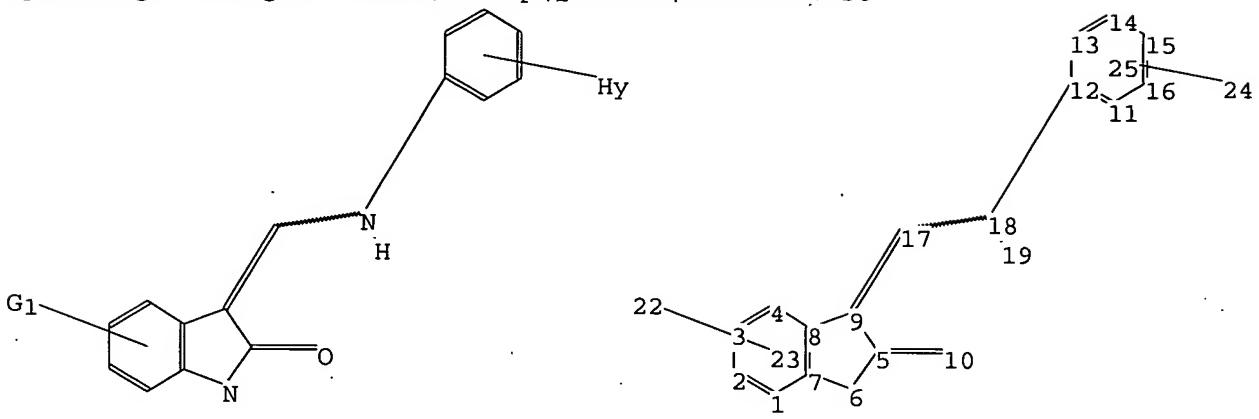
=> s l4 sss full
FULL SEARCH INITIATED 11:42:14 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 3658 TO ITERATE

100.0% PROCESSED 3658 ITERATIONS 2057 ANSWERS

SEARCH TIME: 00.00.01

L6 2057 SEA SSS FUL L4

=>
Uploading C:\Program Files\Stnexp\Queries\10783325b.str



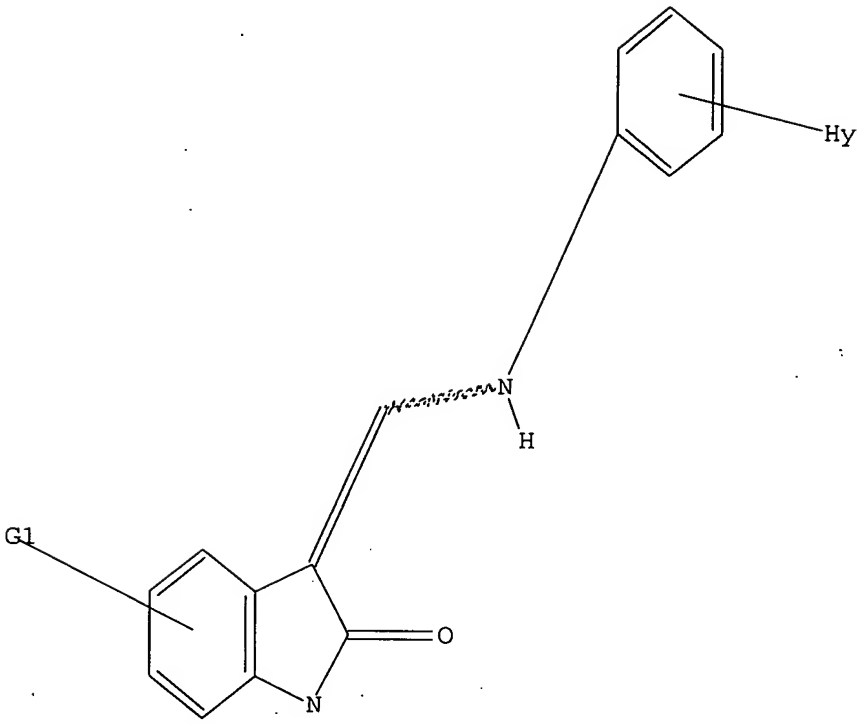
chain nodes :
10 17 18 19 22 24
ring nodes :
1 2 3 4 5 6 7 8 9 11 12 13 14 15 16
chain bonds :
5-10 9-17 12-18 17-18 18-19
ring bonds :
1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 11-12 11-16 12-13 13-14 14-15
15-16
exact/norm bonds :
5-6 5-10 6-7 12-18 17-18
exact bonds :
5-9 8-9 9-17 18-19
normalized bonds :
1-2 1-7 2-3 3-4 4-8 7-8 11-12 11-16 12-13 13-14 14-15 15-16
isolated ring systems :
containing 1 : 11 :

G1:X,CH3,CN,NO2,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
22:CLASS 23:CLASS 24:Atom 25:CLASS

L7 STRUCTURE UPLOADED

=> d l7
L7 HAS NO ANSWERS
L7 STR



G1 X,Me,CN,NO2,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l7
SAMPLE SEARCH INITIATED 11:44:42 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 177 TO ITERATE

100.0% PROCESSED 177 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2742 TO 4338
PROJECTED ANSWERS: 5 TO 234

L8 5 SEA SSS SAM L7

=> s l7 sss full
FULL SEARCH INITIATED 11:44:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 3609 TO ITERATE

100.0% PROCESSED 3609 ITERATIONS 82 ANSWERS

SEARCH TIME: 00.00.01

L9 82 SEA SSS FUL L7

=> FIL CAPLUS

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	487.00	487.21

FILE 'CAPLUS' ENTERED AT 11:45:35 ON 20 JUN 2005
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Jun 2005 VOL 142 ISS 26
FILE LAST UPDATED: 19 Jun 2005 (20050619/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l9
L10 14 L9

=> s l10 and py<=2001
21607156 PY<=2001
L11 7 L10 AND PY<=2001

=> d l10 ibib abs tot

L10 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:965067 CAPLUS
DOCUMENT NUMBER: 141:406039
TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis
INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424
WO 2004096224	A3	20041216		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1473043	A1	20041103	EP 2003-9587	20030429

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:

EP 2003-9587	A	20030429
EP 2004-508	A	20040113
EP 2004-1171	A	20040121

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

L10 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:267298 CAPLUS
DOCUMENT NUMBER: 140:303523
TITLE: Preparation of heterocyclically substituted indolinones as inhibitors of various receptor tyrosine kinases
INVENTOR(S): Kley, Joerg; Heckel, Armin; Hilberg, Frank; Roth, Gerald Juergen; Lehmann-Lintz, Thorsten; Lotz, Ralf R. H.; Tontsch-Grunt, Ulrike; Van Meel, Jacobus C. A.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 226 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

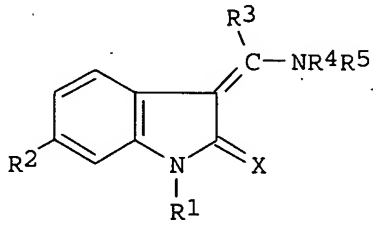
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026829	A2	20040401	WO 2003-EP9978	20030909
WO 2004026829	A3	20041007		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

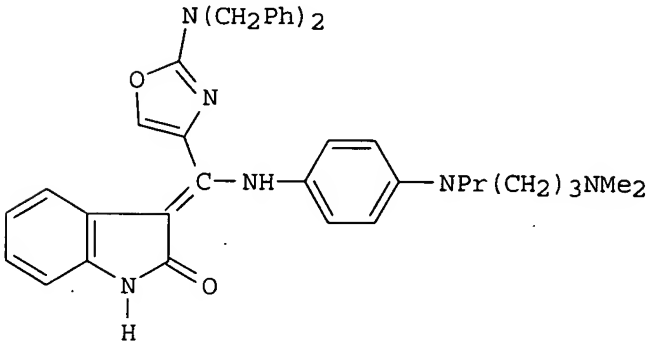
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10242350	A1	20040318	DE 2002-10242350	20020912
DE 10252969	A1	20040527	DE 2002-10252969	20021114
PRIORITY APPLN. INFO.:			DE 2002-10242350	A 20020912
			DE 2002-10252969	A 20021114

OTHER SOURCE(S): MARPAT 140:303523
GI



I



II

AB Title compds. I [X = O, S; R1 = H, prodrug residue, such as alkoxycarbonyl, acyl; R2 = H, F, Cl, Br, CN, NO2, (un)substituted CO2H, CONH2: R3 = (un)substituted 5-6-membered heteroaryl; R4 = (un)substituted cycloalkyl, aryl; R5 = H, alkyl] were prepared I exhibit an inhibiting action on various receptor tyrosine kinases and cyclin-CDK complexes and on the proliferation of endothelial cells and various tumor cells. Thus, 1-acetyl-2-indolinone was treated with 2-dibenzylaminooxazole-4-carboxylic acid to give 1-acetyl-3-{1-hydroxy-1-[2-dibenzylaminooxazol-4-yl]methylene}-2-indolinone which was treated with Me2N(CH2)3NPrC6H4NH2-4 to give the title compound II which had IC50 for inhibition of cell proliferation of 1 nM.

L10 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:218460 CAPLUS
DOCUMENT NUMBER: 140:270851
TITLE: Preparation of heteroaryl-substituted aminomethylideneindolinones as cell proliferation

inhibitors.

INVENTOR(S): Kley, Joerg; Heckel, Armin; Roth, Gerald Juergen; Lehmann-Lintz, Thorsten; Lotz, Ralf; Hilberg, Frank; Tontsch-Grunt, Ulrike; Van Meel, Jacobus

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany

SOURCE: Ger. Offen., 114 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10242350	A1	20040318	DE 2002-10242350	20020912
US 2005054710	A1	20050310	US 2003-656863	20030905
WO 2004026829	A2	20040401	WO 2003-EP9978	20030909
WO 2004026829	A3	20041007		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

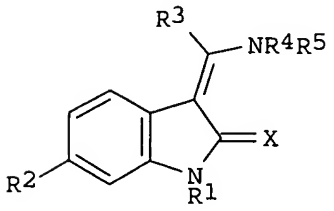
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

DE 2002-10242350	A	20020912
US 2002-414938P	P	20020930
DE 2002-10252969	A	20021114
US 2002-430790P	P	20021204

OTHER SOURCE(S): MARPAT 140:270851

GI



I

AB Title compds. [I; X = O, S; R1 = H, alkoxycarbonyl, alkanoyl, other prodrug residue; R2 = H, F, Cl, Br, cyano, NO2, CO2H, alkoxycarbonyl, cycloalkoxycarbonyl, etc.; R3 = (Ph-condensed) 5-6 membered heteroaryl, etc.; R4 = (imino-interrupted) (substituted) cycloalkyl; R5 = H, alkyl], were prepared 1-Acetyl-3-[1-methoxy-1-(2-dibenzylamino-4-oxazolyl)methylene]-2-indolinone and N-propionyl-N-(3-dimethylaminopropyl)-p-phenylenediamine were heated in DMF at 120° for 3 h; the cooled mixture was treated with aqueous NaOH/MeOH followed by stirring for 1 h to give 31% 3-(Z)-[1-[4-[N-propionyl-N-(3-dimethylaminopropyl)amino]phenylamino]-1-(2-dibenzylamino-4-oxazolyl)methylene]-2-indolinone. I inhibited HUVEC cell proliferation with IC50 = 0.2-120 nM.

L10 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:138723 CAPLUS
DOCUMENT NUMBER: 140:193052
TITLE: Use of LCK inhibitors for treatment of immunological diseases
INVENTOR(S): Roth, Gerald Jurgen; Heckel, Armin; Walter, Rainer; Hilberg, Frank; Hauptmann, Rudolf; Ernst, Steffen; Stefanic, Martin; Colbatzky, Florian
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10237423	A1	20040219	DE 2002-10237423	20020816
CA 2495350	AA	20040304	CA 2003-2495350	20030811
WO 2004017948	A2	20040304	WO 2003-EP8890	20030811
WO 2004017948	A3	20040422		
WO 2004017948	C1	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1530466	A2	20050518	EP 2003-792292	20030811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004204458	A1	20041014	US 2003-640926	20030814
PRIORITY APPLN. INFO.:			DE 2002-10237423 A	20020816
			US 2002-409204P P	20020909
			WO 2003-EP8890 W	20030811

AB The invention discloses a method for treatment of immunol. diseases or pathol. conditions which contain an immunol. component, using certain LCK inhibitors, which already are known as kinase inhibitors for therapy in oncol., optionally in combination with one or more other medications selected from NSAIDs, steroids, DMARDs, immunosuppressants, biol. response modifiers, and antiinfectives. Also disclosed are pharmaceutical compns. which contain the LCK inhibitors as well as the other medications, and use of LCK inhibitors for production of a pharmaceutical composition for treatment of immunol. diseases or pathol. conditions which contain an immunol. component.

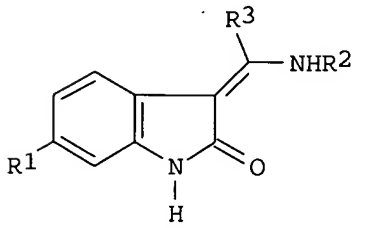
L10 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:80649 CAPLUS
DOCUMENT NUMBER: 140:146001
TITLE: Preparation of indoline derivatives substituted in position 6 as antitumor agents
INVENTOR(S): Roth, Gerald Juergen; Heckel, Armin; Kley, Joerg; Lehmann-Lintz, Thorsten; Hilberg, Frank;

PATENT ASSIGNEE(S): Tontsch-Grunt, Ulrike; Van Meel, Jacobus C. A.
Boehringer Ingelheim Pharma Gmbh & Co. Kg, Germany
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009547	A1	20040129	WO 2003-EP7961	20030722
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10233366	A1	20040212	DE 2002-10233366	20020723
DE 10328533	A1	20050217	DE 2003-10328533	20030624
CA 2493436	AA	20040129	CA 2003-2493436	20030722
US 2005043389	A1	20050224	US 2003-625101	20030722
EP 1523473	A1	20050420	EP 2003-765079	20030722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012799	A	20050503	BR 2003-12799	20030722

PRIORITY APPLN. INFO.:
DE 2002-10233366 A 20020723
US 2002-403106P P 20020813
DE 2003-10328533 A 20030624
WO 2003-EP7961 W 20030722

OTHER SOURCE(S): MARPAT 140:146001
GI



I

AB Indolines I [R1 = F, Cl, Br, CN; R2, R3 = (un)substituted Ph], the tautomers, enantiomers thereof, the mixts. and salts thereof, were prepared for use as inhibitors of various receptor tyrosine kinases and of the proliferation of endothelial cells and various tumor cells (no data). Thus, 2,5-F2C6H3NO2 was treated with CH2(CO2Me)2, decarboxylated and cyclized to 6-fluoro-2-indolinone which was N-acetylated and treated with 3-IC6H4CO2H to give 1-acetyl-3-[1-hydroxy-1-(3-iodophenyl)methylene]-6-chloro-2-indolinone. The latter compound was O-methylated and treated with

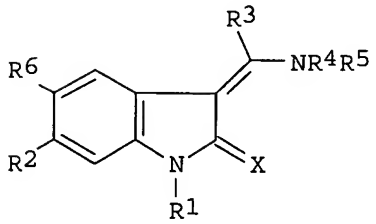
MeSO2NMeC6H4NH2-4 to give I [R1 = Cl, R2 = C6H4NMeSO2Me-4, R2 = C6H4I-3].
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:80648 CAPLUS
DOCUMENT NUMBER: 140:146000
TITLE: Preparation of indoline derivatives substituted in position 6 as antitumor agents
INVENTOR(S): Roth, Gerald Juergen; Heckel, Armin; Kley, Joerg; Lehmann-Lintz, Thorsten; Hilberg, Frank; Tontsch-Grunt, Ulrike; Van Meel, Jacobus
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Gmbh & Co. Kg, Germany
SOURCE: PCT Int. Appl., 355 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009546	A1	20040129	WO 2003-EP7960	20030722
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10233366	A1	20040212	DE 2002-10233366	20020723
CA 2493721	AA	20040129	CA 2003-2493721	20030722
EP 1527046	A1	20050504	EP 2003-765078	20030722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: DE 2002-10233366 A 20020723
WO 2003-EP7960 W 20030722

OTHER SOURCE(S): MARPAT 140:146000
GI



I

AB Indolines I [X = O, S; R1 = H, alkoxycarbonyl, acyl, (un)substituted CH2NH2; R2 = F, Cl, Br, CN; R3 = (un)substituted Ph, naphthyl; R4 =

benzopyrazolyl, (un)substituted cycloalkyl, Ph, naphthyl, heteroaryl; R5 = H, alkyl; R6 = H, NO2], the tautomers, enantiomers, diastereomers thereof, the mixts. and salts thereof, were prepared for use as inhibitors of various receptor tyrosine kinases and of the proliferation of endothelial cells and various tumor cells(no data). Thus, 6-chloro-2-indolinone was N-acetylated and treated with PhC(OEt)3 to give 1-acetyl-3-(1-ethoxy-1-phenylmethylene)-6-chloro-2-indolinone which was treated with Me2NCH2CH2N(SO2Me)C6H4NH2-4 to give I [X = O, R1, R5, R6 = H, R2 = Cl, R3 = Ph, R4 = C6H4N(SO2Me)CH2CH2NMe2-4].

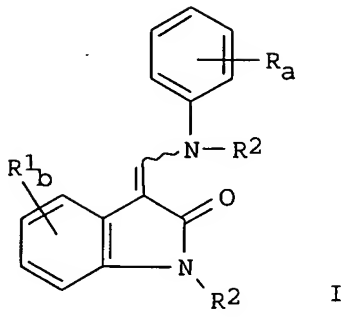
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:261836 CAPLUS
DOCUMENT NUMBER: 138:287525
TITLE: Preparation of 3-(arylamino)methylene-1,3-dihydro-2H-indol-2-ones as tyrosine kinase inhibitors for regulating, modulating and/or inhibiting abnormal cell proliferation
INVENTOR(S): Andrews, Steven W.; Wurster, Julie A.; Hull, Clarence E., III; Wang, Edward H.; Malone, Thomas
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003027102	A1	20030403	WO 2002-US30882	20020927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2461812	AA	20030403	CA 2002-2461812	20020927
US 20031994[illegible]8	A1	20031023	US 2002-256879	20020927
US 6765012	B2	20040720		
US 2003225152	A1	20031204	US 2002-259703	20020927
EP 1430048	A1	20040623	EP 2002-776036	20020927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005508336	T2	20050331	JP 2003-530690	20020927
US 2004198720	A1	20041007	US 2004-783325	20040220

PRIORITY APPLN. INFO.:	US 2001-325815P	P 20010927
	US 2001-325819P	P 20010927
	US 2002-256879	A3 20020927
	WO 2002-US30882	W 20020927

OTHER SOURCE(S): MARPAT 138:287525
GI



I

AB The present invention relates to 3-(arylamino)methylene-1,3-dihydro-2H-indol-2-ones (shown as I; variables defined below; e.g. 3-[(4-morpholinophenylamino)methylene]-1,3-dihydroindol-2-one), capable of modulating tyrosine kinase signal transduction to regulate, modulate and/or inhibit abnormal cell proliferation. For I: R1 = halogen, NO2, CN, C1-C4 alkyl and aryl; R2 = H, C1-C8 alkyl, COCH3, CH2CH2OH, CH2CH2CH2OH and phenyl; R = D, halogen, C1-C8 alkyl, CF3, OCF3, OCF2H, CH2CN, CN, SR2, (CR7R8)cC(O)OR2, C(O)N(R2)2, (CR7R8)cOR2, HNC(O)R2, HNC(O)OR2, (CR7R8)cN(R2)2, SO2(CR7R8)cN(R2)2, OP(O)(OR2)2, OC(O)OR2, OCH2O, HNCH:CH, -N(COR2)CH2CH2, HC:NNH, N:CHS, O(CR7R8)dR6, (CR7R8)cR6 and NR2(CR7R8)dR6. B = 0-3; a = 0-5; c = 0-4; d = 2-5; the wavy line = a E or Z bond; addnl. definitions are given in the claims. Inhibitory biol. data are presented for ≤323 examples of I for the following assays: VEGF stimulated calcium ion signal in vitro, KDR, VEGF-induced dermal extravasation in guinea pig (Miles Assay), and laser-induced choroidal neovascularization in rat. Although the methods of preparation are not claimed, .apprx.80 example prepns. are included.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:283925 CAPLUS
DOCUMENT NUMBER: 134:311105
TITLE: Preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation
INVENTOR(S): Heckel, Armin; Roth, Gerald Juergen; Walter, Rainer; Van Meel, Jacobus; Redemann, Norbert; Tontsch-Grunt, Ulrike; Spevak, Walter; Hilberg, Frank
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 282 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027081	A1	20010419	WO 2000-EP9867	20001009

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19949208	A1	20010419	DE 1999-19949208	19991013
DE 10042696	A1	20020314	DE 2000-10042696	20000831
US 6762180	B1	20040713	US 2000-678682	20001003
CA 2387013	AA	20010419	CA 2000-2387013	20001009
BR 2000014735	A	20020716	BR 2000-14735	20001009
EP 1224170	A1	20020724	EP 2000-971347	20001009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003511441	T2	20030325	JP 2001-530102	20001009
EE 200200197	A	20030616	EE 2002-197	20001009
NZ 518489	A	20050527	NZ 2000-518489	20001009
BG 106587	A	20030131	BG 2002-106587	20020405
ZA 2002002764	A	20040421	ZA 2002-2764	20020409
NO 2002001719	A	20020411	NO 2002-1719	20020411

PRIORITY APPLN. INFO.:

DE 1999-19949208	A	19991013
DE 2000-10042696	A	20000831
US 1999-160547P	P	19991020
WO 2000-EP9867	W	20001009

OTHER SOURCE(S): MARPAT 134:311105
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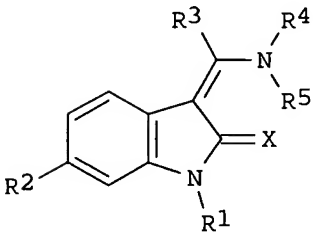

I

AB The invention relates to the preparation of substituted (Z)-aminomethyleneindolines I [wherein X = O or S; R1 = H, C1-4 alkoxycarbonyl, C2-4 alkanoyl; R2 = HO2C, C1-6 alkoxycarbonyl, C4-7 cycloalkoxycarbonyl, aryloxycarbonyl, aminocarbonyl, or alkyl-substituted aminocarbonyl; R3 = H, C1-6 alkyl, C3-7 cycloalkyl, CF3, heteroaryl, or (un)substituted Ph or naphthyl; R4 and R5 = independently C3-7 cycloalkyl, monosubstituted phenyl] isomers and salts thereof as receptor tyrosine kinase and cyclin/CDK complex inhibitors for the treatment of endothelial cells and tumor cell proliferation. For example, 1-acetyl-6-ethoxycarbonyl-3-(ethoxyphenylmethylene)-2-indolinone and N-(4-aminophenyl)-N-(3-dimethylaminopropyl)acetamide were stirred together in DMF at 100° for 3h followed by addition of piperidine to give I (X = O; R1 = H; R2 = EtO2C; R3 = EtO; R4 = (Me2NCH2CH2CH2)N(Ac)C6H4; R5 = H). I inhibited the proliferation of endothelial cells with an IC50 of 0.003 μM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:688216 CAPLUS
DOCUMENT NUMBER: 133:266726

TITLE: Preparation of 3-(anilinomethylene)oxindoles and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors

INVENTOR(S): Glennon, Kimberley Caroline; Kuyper, Lee Frederick; Lackey, Karen Elizabeth; McNutt, Robert Walton, Jr.

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056710	A1	20000928	WO 2000-US5057	20000228
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165514	A1	20020102	EP 2000-913643	20000228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6350747	B1	20020226	US 2000-514528	20000228
JP 2002540097	T2	20021126	JP 2000-606572	20000228
US 6498176	B1	20021224	US 2001-914063	20010822
US 2002099071	A1	20020725	US 2001-966318	20010927
US 6818632	B2	20041116		
US 2004191210	A1	20040930	US 2003-742435	20031219

PRIORITY APPLN. INFO.:		
GB 1999-4933	A	19990304
US 2000-514528	A3	20000228
WO 2000-US5057	W	20000228
US 2001-966318	A3	20010927

OTHER SOURCE(S): MARPAT 133:266726

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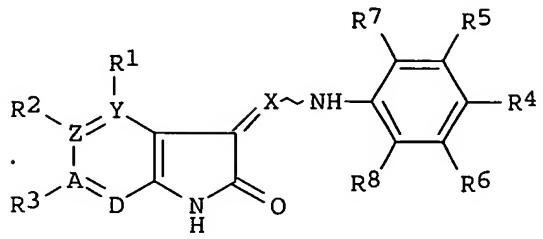

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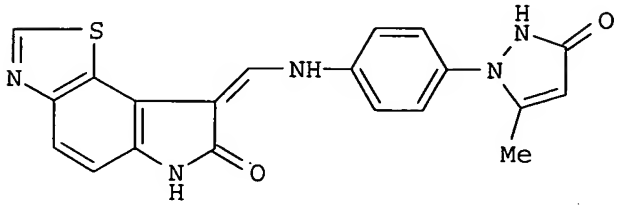

II

AB The title compds. (I) [wherein X = N, CH, CCF3, or C(aliphatic); Y, Z, A, and D = C or N, and the number of N ≤ 1; R1 = H, aliphatic, SH, hydroxy(aliphatic), aryl(aliphatic), cycloalkyl(aliphatic), heterocyclyl(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxycarbonyl, halo, CN, or NO2; R2 = H, aliphatic, hydroxyimino aliphatic, alkoxy(carbonyl), hydroxyaliph., aryl(oxycarbonyl), heterocyclyl, (un)substituted CONH2, NH2, or SO2NH2, halo, OH, NO2, aliphatic sulfonyl, etc.; or R1 and R2 are joined to form an (un)substituted fused heterocyclic ring; R3 = H, aliphatic, hydroxy(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxy, aryl(oxy), hydroxyaryl, (hydroxy)heterocyclyl, heterocyclyloxy, or halo; or R2 and R3 are joined to form an (un)substituted fused heterocyclic ring; R4 = SO3H, (aliphatic)sulfonyl(aliphatic), (un)substituted SO2NH2, NH2, CONH2, etc.; R5 = H; or R4 and R5 are joined to form an (un)substituted fused heterocyclic ring] were prepared via standard synthetic methods and solution phase library techniques as vascular endothelial growth factor receptor type 2 (VEGFR-2), cyclin dependent kinase 2 (CDK2), tyrosine kinase Tie-2 receptor, and colony-stimulating factor 1 receptor kinase (c-fms) inhibitors. For example, a mixture of 8-dimethylaminomethylene-6,8-dihydro-1-thia-3,6-diaza-as-indacene-7-one (preparation given) and 2-(4-aminophenyl)-3-methylpyrazolin-5-one in absolute EtOH was heated with stirring at 90°C for 16 h to give (Z)-II (83%). In substrate phosphorylation assays, II inhibited VEGFR-2 and CDK2 with IC50 values of 1-10 μM and 11-50 μM, resp. I are useful as therapeutic agents in disease states alleviated by the inhibition or antagonism of protein kinase activated signalling pathways in general, and in particular in the pathol. processes which involve aberrant cellular proliferation, such as tumor growth, restenosis, atherosclerosis, and thrombosis. I are particularly useful for suppressing tumor growth by inhibiting tumor-related angiogenesis.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:227630 CAPLUS
DOCUMENT NUMBER: 132:265083
TITLE: Preparation of 3-aminobenzylideneindolinones as cyclin dependent kinase inhibitors
INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin;

Himmelsbach, Frank; Eberlein, Wolfgang; Roth, Gerald; Van Meel, Jacobus C. A.; Redemann, Norbert; Spevak, Walter; Tontsch-Grunt, Ulrike; Von Ruden, Thomas

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 269 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19844003	A1	20000330	DE 1998-19844003	19980925
DE 19937496	A1	20010215	DE 1999-19937496	19990807
CA 2342622	AA	20000406	CA 1999-2342622	19990922
AU 9960863	A1	20000417	AU 1999-60863	19990922
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922
EP 1115704	B1	20030618		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002525356	T2	20020813	JP 2000-572194	19990922
EE 200100184	A	20020815	EE 2001-184	19990922
AT 243195	E	20030715	AT 1999-947404	19990922
NZ 510845	A	20031031	NZ 1999-510845	19990922
BG 105327	A	20011231	BG 2001-105327	20010309
HR 2001000216	A1	20020430	HR 2001-216	20010321
NO 2001001477	A	20010322	NO 2001-1477	20010322
US 2004058978	A1	20040325	US 2003-666643	20030919
US 6855710	B2	20050215		

PRIORITY APPLN. INFO.:

DE 1998-19844003	A	19980925
DE 1999-19937496	A	19990807
WO 1999-EP7040	W	19990922
US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:265083

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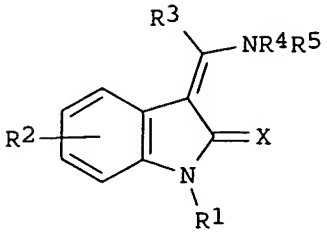

I

AB Title compds. [I; R1 = H, OH, alkyl; R2 = H, halo, NO2, alkyl; R3 = (un)substituted Ph or -naphthyl; R4 = H or alkyl; R5 = (un)substituted alkylphenyl or -alkylnaphthyl; X = O or S] were prepared Thus, 2-indolinone was N-acetyltated and the product condensed with PhC(OEt)3 to give, after PhNH2 treatment, I (R1 = R2 = R4 = H, R3 = R5 = Ph, X = O). Data for biol. activity of I were given.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:206644 CAPLUS
DOCUMENT NUMBER: 132:251076
TITLE: Preparation of aminoarylmethylideneindolinones as kinase inhibitors.
INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin; Himmelsbach, Frank; Eberlein, Wolfgang; Van Meel, Jakobus; Redemann, Norbert; Spevak, Walter; Tontsch-Grunt, Ulrike; Von Rueden, Thomas
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 66 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19844003	A1	20000330	DE 1998-19844003	19980925
CA 2342622	AA	20000406	CA 1999-2342622	19990922
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960863	A1	20000417	AU 1999-60863	19990922
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922
EP 1115704	B1	20030618		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100854	T2	20011221	TR 2001-200100854	19990922

JP 2002525356	T2	20020813	JP 2000-572194		19990922
EE 200100184	A	20020815	EE 2001-184		19990922
AT 243195	E	20030715	AT 1999-947404		19990922
NZ 510845	A	20031031	NZ 1999-510845		19990922
PT 1115704	T	20031128	PT 1999-947404		19990922
ES 2196860	T3	20031216	ES 1999-947404		19990922
BG 105327	A	20011231	BG 2001-105327		20010309
ZA 2001002260	A	20040419	ZA 2001-2260		20010319
HR 2001000216	A1	20020430	HR 2001-216		20010321
NO 2001001477	A	20010322	NO 2001-1477		20010322
US 2004058978	A1	20040325	US 2003-666643		20030919
US 6855710	B2	20050215			
PRIORITY APPLN. INFO.:			DE 1998-19844003	A	19980925
			DE 1999-19937496	A	19990807
			WO 1999-EP7040	W	19990922
			US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:251076
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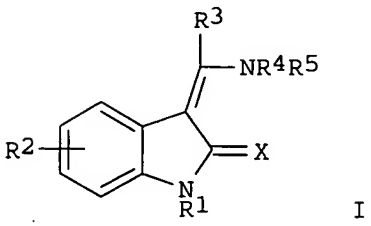

I

AB Title compds. [I; X = O, S; R1 = H, alkyl; R2 = H, F, Cl, Br, iodo, alkyl, NO2; R3 = (substituted) Ph, naphthyl; R4 = H, alkyl; R5 = (substituted) Ph, naphthyl], were prepared Thus, (Z)-3-[1-(4-piperidinomethylphenylamino)-1-phenylmethylidene]-5-nitro-2-indolinone [prepared from 3-(1-ethoxy-1-phenylmethylidene)-5-nitro-2-indolinone and 4-piperidinomethylaniline in DMF] inhibited proliferation of SCUT 1B tumor proliferation in mice with IC50 = 0.22 μM.

L10 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:784079 CAPLUS
DOCUMENT NUMBER: 132:12258
TITLE: Aminomethyleneindolinones with antitumor activity
INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Norbert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962882	A1	19991209	WO 1999-EP3692	19990528

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,

MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19824922	A1	19991209	DE 1998-19824922		19980604
CA 2328291	AA	19991209	CA 1999-2328291		19990528
AU 9943707	A1	19991220	AU 1999-43707		19990528
AU 764782	B2	20030828			
BR 9910898	A	20010213	BR 1999-10898		19990528
EP 1100779	A1	20010523	EP 1999-926454		19990528
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TR 200003515	T2	20010621	TR 2000-200003515		19990528
EE 200000723	A	20020415	EE 2000-723		19990528
JP 2002516906	T2	20020611	JP 2000-552094		19990528
US 6319918	B1	20011120	US 1999-323499		19990601
ZA 2000005435	A	20020107	ZA 2000-5435		20001005
BG 104938	A	20010629	BG 2000-104938		20001113
NO 2000006138	A	20010201	NO 2000-6138		20001201
HR 2000000831	A1	20011231	HR 2000-831		20001201
US 6545035	B1	20030408	US 2001-969912		20011003
PRIORITY APPLN. INFO.:			DE 1998-19824922	A	19980604
			US 1998-92014P	P	19980708
			WO 1999-EP3692	W	19990528
			US 1999-323499	A3	19990601

OTHER SOURCE(S): MARPAT 132:12258
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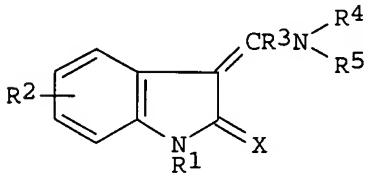

I

AB Title compds. I [X = O, S; R1 = H, alkoxycarbonyl, alkanoyl; R2 = CO2H, alkoxycarbonyl, (un)substituted CONH2; R3 = H, (un)substituted alkyl; R4 = H, (un)substituted alkyl, Ph, naphthyl, heteroaryl; R5 = H, alkyl] were prepared Thus, 2-oxo-5-indolinecarboxylic acid was attached to Rink resin and treated with tri-Me orthovalerate to give polymer-bound 3-Z-(1-methoxy-1-butylmethylene)-2-oxo-5-indolinecarboxamide which was treated with 4-piperidinomethylaniline to give I [X = O, R1 = 5-CONH2, R2, R4 = h, R3 = Bu, R5 = 4-piperidinomethylanilino]. This compound had an IC50 for inhibition of SKUT-1B cell proliferation of 0.036 μM.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:672749 CAPLUS
DOCUMENT NUMBER: 131:299364
TITLE: Substituted indolinones having an inhibiting effect on kinases and cyclin/CDK complexes
INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Robert

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952869	A1	19991021	WO 1999-EP2436	19990410
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19816624	A1	19991021	DE 1998-19816624	19980415
US 6169106	B1	20010102	US 1999-286983	19990406
CA 2323111	AA	19991021	CA 1999-2323111	19990410
AU 9938149	A1	19991101	AU 1999-38149	19990410
AU 749829	B2	20020704		
BR 9909688	A	20001219	BR 1999-9688	19990410
EP 1071665	A1	20010131	EP 1999-920635	19990410
EP 1071665	B1	20031001		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200002980	T2	20010221	TR 2000-200002980	19990410
EE 200000598	A	20020415	EE 2000-598	19990410
EE 4432	B1	20050215		
JP 2002511449	T2	20020416	JP 2000-543432	19990410
NZ 507967	A	20030429	NZ 1999-507967	19990410
AT 251138	E	20031015	AT 1999-920635	19990410
SK 283824	B6	20040203	SK 2000-1513	19990410
PT 1071665	T	20040227	PT 1999-920635	19990410
ES 2207209	T3	20040516	ES 1999-920635	19990410
TW 510897	B	20021121	TW 1999-88105963	19990414
ZA 2000004623	A	20010307	ZA 2000-4623	20000904
BG 104813	A	20010831	BG 2000-104813	20000929
BG 64443	B1	20050228		
NO 2000005151	A	20001013	NO 2000-5151	20001013
PRIORITY APPLN. INFO.:			DE 1998-19816624 A	19980415
			US 1998-90227P P	19980622
			WO 1999-EP2436 W	19990410

OTHER SOURCE(S): MARPAT 131:299364
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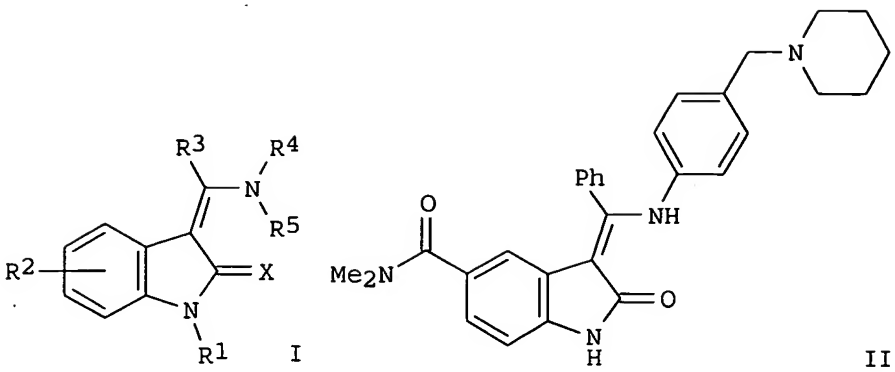

I II

AB The invention relates to substituted indolinones I [X = O or S; R1 = H, alkoxycarbonyl, alkanoyl; R2 = CO2H, alkoxycarbonyl, or (di)(alkyl)aminocarbonyl; R3 = (un)substituted Ph or naphthyl; R4 = H, alkyl; R5 = H, (un)substituted alkyl, cycloalkyl, indanyl, Ph, heteroaryl, pyrrolidinyl, or piperidinyl], their isomers, and their salts, especially their physiol. compatible salts. The compds. have valuable pharmacol. properties, especially an inhibitory effect on various kinases and cyclin/CDK complexes, and on the proliferation of various tumor cells. The invention also relates to medicaments containing the compds., to their use, and to methods for producing them. Approx. 160 example compds. and 7 pharmaceutical formulations are described. For instance, title compound II was prepared from 2-indolinone-5-carboxylic acid Me ester in 5 steps: (1) N-acetylation (86%); (2) condensation with PhC(OEt)3 to give the 3-(1-ethoxy-1-phenylmethylene) derivative (67%); (3) condensation of the alkoxymethylene compound with a corresponding amine and deacetylation; (4) saponification of the Me ester; and (5) amidation of the resulting acid with dimethylamine (88%). In an assay against SK-UT-1B lung tumor cells in mice, II had an IC50 value of 0.01 μM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:659664 CAPLUS
DOCUMENT NUMBER: 131:271809
TITLE: Preparation of 3-(α-heteroarylaminobenzylidene)-2-indolinones as Cyclin dependent kinase inhibitors
INVENTOR(S): Grell, Wolfgang; Walter, Rainer; Heckel, Armin; Himmelsbach, Frank; Wittneben, Helmut; van Meel, Jakobus; Redemann, Norbert; Haigh, Robert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 64 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19815020	A1	19991007	DE 1998-19815020	19980403
US 6043254	A	20000328	US 1999-277063	19990326
WO 9951590	A1	19991014	WO 1999-EP2186	19990330

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9937034	A1	19991025	AU 1999-37034		19990330
PRIORITY APPLN. INFO.:			DE 1998-19815020	A	19980403
			US 1998-86733P	P	19980526
			WO 1999-EP2186	W	19990330

OTHER SOURCE(S): MARPAT 131:271809
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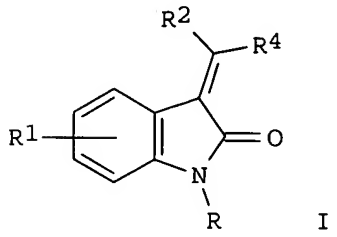

I

AB Title compds. [I; R = H; R1 = H, halo, NO2, (alkanoyl)amino, etc.; R2 = (un)substituted Ph; R4 = NHR3; R3 = heteroannelated Ph, heteroarylalk(en)ylphenyl, etc.] were prepared Thus,2-indolinone was N-acetylated and the product condensed with PhC(OEt)3 to give I (R1 = H, R2 = Ph)(II; R = Ac, R4 = OEt) which was condensed with 5-aminoindole to give II (R = H, R4 = 5-indolylamino). Data for biol. activity of I were given.

=> d l11 ibib abs tot

L11 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:283925 CAPLUS
DOCUMENT NUMBER: 134:311105
TITLE: Preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation
INVENTOR(S): Heckel, Armin; Roth, Gerald Juergen; Walter, Rainer; Van Meel, Jacobus; Redemann, Norbert; Tontsch-Grunt, Ulrike; Spevak, Walter; Hilberg, Frank
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 282 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001027081	A1	20010419	WO 2000-EP9867		20001009 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
DE 19949208	A1	20010419	DE 1999-19949208		19991013 <--
DE 10042696	A1	20020314	DE 2000-10042696		20000831
US 6762180	B1	20040713	US 2000-678682		20001003
CA 2387013	AA	20010419	CA 2000-2387013		20001009 <--
BR 2000014735	A	20020716	BR 2000-14735		20001009
EP 1224170	A1	20020724	EP 2000-971347		20001009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003511441	T2	20030325	JP 2001-530102		20001009
EE 200200197	A	20030616	EE 2002-197		20001009
NZ 518489	A	20050527	NZ 2000-518489		20001009
BG 106587	A	20030131	BG 2002-106587		20020405
ZA 2002002764	A	20040421	ZA 2002-2764		20020409
NO 2002001719	A	20020411	NO 2002-1719		20020411
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			DE 2000-10042696	A	20000831
			US 1999-160547P	P	19991020
			WO 2000-EP9867	W	20001009

OTHER SOURCE(S): MARPAT 134:311105

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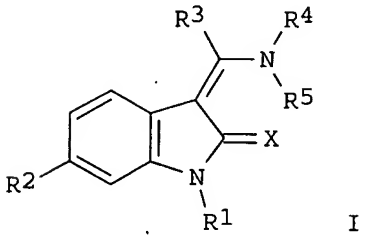

I

AB The invention relates to the preparation of substituted (Z)-aminomethyleneindolines I [wherein X = O or S; R1 = H, C1-4 alkoxycarbonyl, C2-4 alkanoyl; R2 = HO2C, C1-6 alkoxycarbonyl, C4-7 cycloalkoxycarbonyl, aryloxycarbonyl, aminocarbonyl, or alkyl-substituted aminocarbonyl; R3 = H, C1-6 alkyl, C3-7 cycloalkyl, CF3, heteroaryl, or (un)substituted Ph or naphthyl; R4 and R5 = independently C3-7 cycloalkyl, monosubstituted phenyl] isomers and salts thereof as receptor tyrosine kinase and cyclin/CDK complex inhibitors for the treatment of endothelial cells and tumor cell proliferation. For example, 1-acetyl-6-ethoxycarbonyl-3-(ethoxyphenylmethylene)-2-indolinone and N-(4-aminophenyl)-N-(3-dimethylaminopropyl)acetamide were stirred together in DMF at 100° for 3h followed by addition of piperidine to give I (X = O; R1 = H; R2 = EtO2C; R3 = EtO; R4 = (Me2NCH2CH2CH2)N(Ac)C6H4; R5 = H). I inhibited the proliferation of endothelial cells with an IC50 of 0.003 μM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:688216 CAPLUS
DOCUMENT NUMBER: 133:266726
TITLE: Preparation of 3-(anilinomethylene)oxindoles and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors
INVENTOR(S): Glennon, Kimberley Caroline; Kuyper, Lee Frederick; Lackey, Karen Elizabeth; McNutt, Robert Walton, Jr.
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056710	A1	20000928	WO 2000-US5057	20000228 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165514	A1	20020102	EP 2000-913643	20000228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6350747	B1	20020226	US 2000-514528	20000228
JP 2002540097	T2	20021126	JP 2000-606572	20000228
US 6498176	B1	20021224	US 2001-914063	20010822
US 2002099071	A1	20020725	US 2001-966318	20010927
US 6818632	B2	20041116		
US 2004191210	A1	20040930	US 2003-742435	20031219

PRIORITY APPLN. INFO.:

GB 1999-4933	A	19990304
US 2000-514528	A3	20000228
WO 2000-US5057	W	20000228
US 2001-966318	A3	20010927

OTHER SOURCE(S): MARPAT 133:266726
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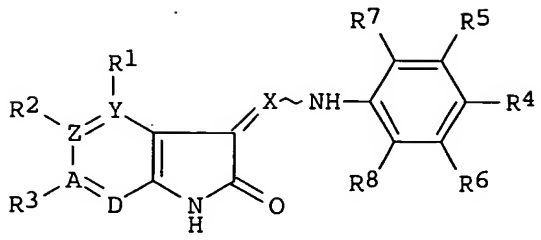

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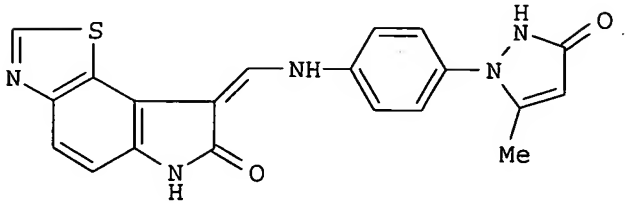

II

AB The title compds. (I) [wherein X = N, CH, CCF3, or C(aliphatic); Y, Z, A, and D = C or N, and the number of N ≤ 1; R1 = H, aliphatic, SH, hydroxy(aliphatic), aryl(aliphatic), cycloalkyl(aliphatic), heterocyclyl(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxycarbonyl, halo, CN, or NO2; R2 = H, aliphatic, hydroxyimino aliphatic, alkoxy(carbonyl), hydroxyaliph., aryl(oxycarbonyl), heterocyclyl, (un)substituted CONH2, NH2, or SO2NH2, halo, OH, NO2, aliphatic sulfonyl, etc.; or R1 and R2 are joined to form an (un)substituted fused heterocyclic ring; R3 = H, aliphatic, hydroxy(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxy, aryl(oxy), hydroxyaryl, (hydroxy)heterocyclyl, heterocyclyloxy, or halo; or R2 and R3 are joined to form an (un)substituted fused heterocyclic ring; R4 = SO3H, (aliphatic)sulfonyl(aliphatic), (un)substituted SO2NH2, NH2, CONH2, etc.; R5 = H; or R4 and R5 are joined to form an (un)substituted fused heterocyclic ring] were prepared via standard synthetic methods and solution phase library techniques as vascular endothelial growth factor receptor type 2 (VEGFR-2), cyclin dependent kinase 2 (CDK2), tyrosine kinase Tie-2 receptor, and colony-stimulating factor 1 receptor kinase (c-fms) inhibitors. For example, a mixture of 8-dimethylaminomethylene-6,8-dihydro-1-thia-3,6-diaza-as-indacene-7-one (preparation given) and 2-(4-aminophenyl)-3-methylpyrazolin-5-one in absolute EtOH was heated with stirring at 90°C for 16 h to give (Z)-II (83%). In substrate phosphorylation assays, II inhibited VEGFR-2 and CDK2 with IC50 values of 1-10 μM and 11-50 μM, resp. I are useful as therapeutic agents in disease states alleviated by the inhibition or antagonism of protein kinase activated signalling pathways in general, and in particular in the pathol. processes which involve aberrant cellular proliferation, such as tumor growth, restenosis, atherosclerosis, and thrombosis. I are particularly useful for suppressing tumor growth by inhibiting tumor-related angiogenesis.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:227630 CAPLUS
DOCUMENT NUMBER: 132:265083
TITLE: Preparation of 3-aminobenzylideneindolinones as cyclin dependent kinase inhibitors
INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin;

Himmelsbach, Frank; Eberlein, Wolfgang; Roth, Gerald; Van Meel, Jacobus C. A.; Redemann, Norbert; Spevak, Walter; Tontsch-Grunt, Ulrike; Von Ruden, Thomas
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 269 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19844003	A1	20000330	DE 1998-19844003	19980925 <--
DE 19937496	A1	20010215	DE 1999-19937496	19990807 <--
CA 2342622	AA	20000406	CA 1999-2342622	19990922 <--
AU 9960863	A1	20000417	AU 1999-60863	19990922 <--
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922 <--
EP 1115704	B1	20030618		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002525356	T2	20020813	JP 2000-572194	19990922
EE 200100184	A	20020815	EE 2001-184	19990922
AT 243195	E	20030715	AT 1999-947404	19990922
NZ 510845	A	20031031	NZ 1999-510845	19990922
BG 105327	A	20011231	BG 2001-105327	20010309 <--
HR 2001000216	A1	20020430	HR 2001-216	20010321
NO 2001001477	A	20010322	NO 2001-1477	20010322 <--
US 2004058978	A1	20040325	US 2003-666643	20030919
US 6855710	B2	20050215		

PRIORITY APPLN. INFO.:

DE 1998-19844003	A	19980925
DE 1999-19937496	A	19990807
WO 1999-EP7040	W	19990922
US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:265083
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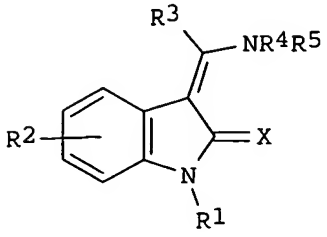

I

AB Title compds. [I; R1 = H, OH, alkyl; R2 = H, halo, NO2, alkyl; R3 = (un)substituted Ph or -naphthyl; R4 = H or alkyl; R5 = (un)substituted alkylphenyl or -alkylnaphthyl; X = O or S] were prepared Thus, 2-indolinone was N-acetyltated and the product condensed with PhC(OEt)3 to give, after PhNH2 treatment, I (R1 = R2 = R4 = H, R3 = R5 = Ph, X = O). Data for biol. activity of I were given.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:206644 CAPLUS
DOCUMENT NUMBER: 132:251076
TITLE: Preparation of aminoarylmethylideneindolinones as kinase inhibitors.
INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin; Himmelsbach, Frank; Eberlein, Wolfgang; Van Meel, Jakobus; Redemann, Norbert; Spevak, Walter; Tontsch-Grunt, Ulrike; Von Rueden, Thomas
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 66 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19844003	A1	20000330	DE 1998-19844003	19980925 <--
CA 2342622	AA	20000406	CA 1999-2342622	19990922 <--
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960863	A1	20000417	AU 1999-60863	19990922 <--
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922 <--
EP 1115704	B1	20030618		
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TR 200100854	T2	20011221	TR 2001-200100854	19990922 <--

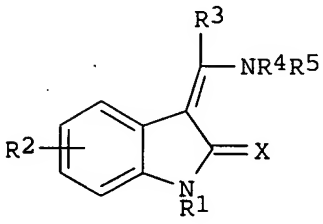
JP 2002525356	T2	20020813	JP 2000-572194	19990922	
EE 200100184	A	20020815	EE 2001-184	19990922	
AT 243195	E	20030715	AT 1999-947404	19990922	
NZ 510845	A	20031031	NZ 1999-510845	19990922	
PT 1115704	T	20031128	PT 1999-947404	19990922	
ES 2196860	T3	20031216	ES 1999-947404	19990922	
BG 105327	A	20011231	BG 2001-105327	20010309	<--
ZA 2001002260	A	20040419	ZA 2001-2260	20010319	
HR 2001000216	A1	20020430	HR 2001-216	20010321	
NO 2001001477	A	20010322	NO 2001-1477	20010322	<--
US 2004058978	A1	20040325	US 2003-666643	20030919	
US 6855710	B2	20050215			

PRIORITY APPLN. INFO.:

DE 1998-19844003	A	19980925
DE 1999-19937496	A	19990807
WO 1999-EP7040	W	19990922
US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:251076

GI



I

AB Title compds. [I; X = O, S; R1 = H, alkyl; R2 = H, F, Cl, Br, iodo, alkyl, NO2; R3 = (substituted) Ph, naphthyl; R4 = H, alkyl; R5 = (substituted) Ph, naphthyl], were prepared Thus, (Z)-3-[1-(4-piperidinomethylphenylamino)-1-phenylmethylidene]-5-nitro-2-indolinone [prepared from 3-(1-ethoxy-1-phenylmethylidene)-5-nitro-2-indolinone and 4-piperidinomethylaniline in DMF] inhibited proliferation of SCUT 1B tumor proliferation in mice with IC50 = 0.22 μM.

L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:784079 CAPLUS
DOCUMENT NUMBER: 132:12258
TITLE: Aminomethyleneindolinones with antitumor activity
INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Norbert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9962882	A1	19991209	WO 1999-EP3692	19990528	<--

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,

MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19824922	A1	19991209	DE 1998-19824922		19980604 <--
CA 2328291	AA	19991209	CA 1999-2328291		19990528 <--
AU 9943707	A1	19991220	AU 1999-43707		19990528 <--
AU 764782	B2	20030828			
BR 9910898	A	20010213	BR 1999-10898		19990528 <--
EP 1100779	A1	20010523	EP 1999-926454		19990528 <--
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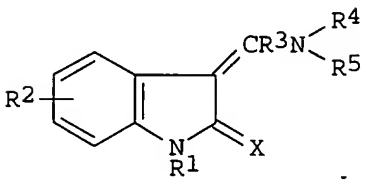
TR 200003515	T2	20010621	TR 2000-200003515		19990528 <--
EE 200000723	A	20020415	EE 2000-723		19990528
JP 2002516906	T2	20020611	JP 2000-552094		19990528
US 6319918	B1	20011120	US 1999-323499		19990601 <--
ZA 2000005435	A	20020107	ZA 2000-5435		20001005
BG 104938	A	20010629	BG 2000-104938		20001113 <--
NO 2000006138	A	20010201	NO 2000-6138		20001201 <--
HR 2000000831	A1	20011231	HR 2000-831		20001201 <--
US 6545035	B1	20030408	US 2001-969912		20011003
PRIORITY APPLN. INFO.:			DE 1998-19824922	A	19980604
			US 1998-92014P	P	19980708
			WO 1999-EP3692	W	19990528
			US 1999-323499	A3	19990601

OTHER SOURCE(S): MARPAT 132:12258
GI



I

AB Title compds. I [X = O, S; R1 = H, alkoxycarbonyl, alkanoyl; R2 = CO2H, alkoxycarbonyl, (un)substituted CONH2; R3 = H, (un)substituted alkyl; R4 = H, (un)substituted alkyl, Ph, naphthyl, heteroaryl; R5 = H, alkyl] were prepared Thus, 2-oxo-5-indolinecarboxylic acid was attached to Rink resin and treated with tri-Me orthovalerate to give polymer-bound 3-Z-(1-methoxy-1-butylmethylene)-2-oxo-5-indolinecarboxamide which was treated with 4-piperidinomethylaniline to give I [X = O, R1 = 5-CONH2, R2, R4 = h, R3 = Bu, R5 = 4-piperidinomethylanilino]. This compound had an IC50 for inhibition of SKUT-1B cell proliferation of 0.036 μM.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:672749 CAPLUS
DOCUMENT NUMBER: 131:299364
TITLE: Substituted indolinones having an inhibiting effect on kinases and cyclin/CDK complexes
INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Robert

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952869	A1	19991021	WO 1999-EP2436	19990410 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19816624	A1	19991021	DE 1998-19816624	19980415 <--
US 6169106	B1	20010102	US 1999-286983	19990406 <--
CA 2323111	AA	19991021	CA 1999-2323111	19990410 <--
AU 9938149	A1	19991101	AU 1999-38149	19990410 <--
AU 749829	B2	20020704		
BR 9909688	A	20001219	BR 1999-9688	19990410 <--
EP 1071665	A1	20010131	EP 1999-920635	19990410 <--
EP 1071665	B1	20031001		
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TR 200002980	T2	20010221	TR 2000-200002980	19990410 <--
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EE 4432	B1	20050215		
JP 2002511449	T2	20020416	JP 2000-543432	19990410
NZ 507967	A	20030429	NZ 1999-507967	19990410
AT 251138	E	20031015	AT 1999-920635	19990410
SK 283824	B6	20040203	SK 2000-1513	19990410
PT 1071665	T	20040227	PT 1999-920635	19990410
ES 2207209	T3	20040516	ES 1999-920635	19990410
TW 510897	B	20021121	TW 1999-88105963	19990414
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BG 104813	A	20010831	BG 2000-104813	20000929 <--
BG 64443	B1	20050228		
NO 2000005151	A	20001013	NO 2000-5151	20001013 <--

PRIORITY APPLN. INFO.:	DE 1998-19816624	A	19980415
	US 1998-90227P	P	19980622
	WO 1999-EP2436	W	19990410

OTHER SOURCE(S): MARPAT 131:299364
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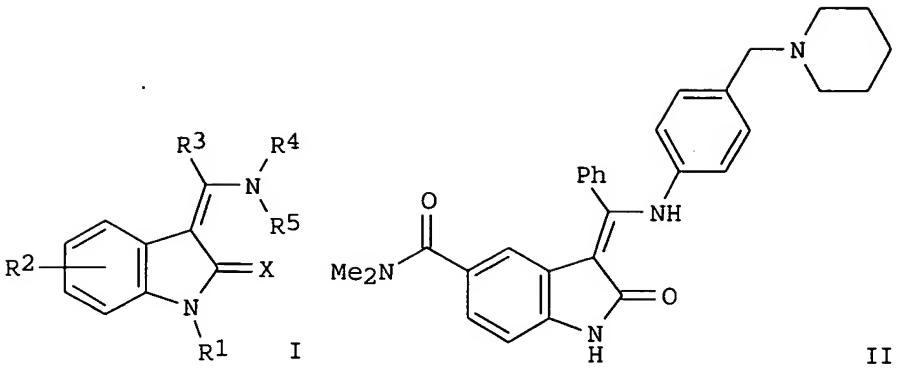

I II

AB The invention relates to substituted indolinones I [X = O or S; R1 = H, alkoxycarbonyl, alkanoyl; R2 = CO2H, alkoxycarbonyl, or (di)(alkyl)aminocarbonyl; R3 = (un)substituted Ph or naphthyl; R4 = H, alkyl; R5 = H, (un)substituted alkyl, cycloalkyl, indanyl, Ph, heteroaryl, pyrrolidinyl, or piperidinyl], their isomers, and their salts, especially their physiol. compatible salts. The compds. have valuable pharmacol. properties, especially an inhibitory effect on various kinases and cyclin/CDK complexes, and on the proliferation of various tumor cells. The invention also relates to medicaments containing the compds., to their use, and to methods for producing them. Approx. 160 example compds. and 7 pharmaceutical formulations are described. For instance, title compound II was prepared from 2-indolinone-5-carboxylic acid Me ester in 5 steps: (1) N-acetylation (86%); (2) condensation with PhC(OEt)3 to give the 3-(1-ethoxy-1-phenylmethylene) derivative (67%); (3) condensation of the alkoxymethylene compound with a corresponding amine and deacetylation; (4) saponification of the Me ester; and (5) amidation of the resulting acid with dimethylamine (88%). In an assay against SK-UT-1B lung tumor cells in mice, II had an IC50 value of 0.01 μM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:659664 CAPLUS
DOCUMENT NUMBER: 131:271809
TITLE: Preparation of 3-(α-heteroarylaminobenzylidene)-2-indolinones as Cyclin dependent kinase inhibitors
INVENTOR(S): Grell, Wolfgang; Walter, Rainer; Heckel, Armin; Himmelsbach, Frank; Wittneben, Helmut; van Meel, Jakobus; Redemann, Norbert; Haigh, Robert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 64 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19815020	A1	19991007	DE 1998-19815020	19980403 <--
US 6043254	A	20000328	US 1999-277063	19990326 <--
WO 9951590	A1	19991014	WO 1999-EP2186	19990330 <--

WO 2001027081	A1	20010419	WO 2000-EP9867		20001009 <--
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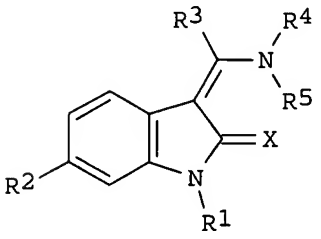
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
DE 19949208	A1	20010419	DE 1999-19949208		19991013 <--
DE 10042696	A1	20020314	DE 2000-10042696		20000831
US 6762180	B1	20040713	US 2000-678682		20001003
CA 2387013	AA	20010419	CA 2000-2387013		20001009 <--
BR 2000014735	A	20020716	BR 2000-14735		20001009
EP 1224170	A1	20020724	EP 2000-971347		20001009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003511441	T2	20030325	JP 2001-530102		20001009
EE 200200197	A	20030616	EE 2002-197		20001009
NZ 518489	A	20050527	NZ 2000-518489		20001009
BG 106587	A	20030131	BG 2002-106587		20020405
ZA 2002002764	A	20040421	ZA 2002-2764		20020409
NO 2002001719	A	20020411	NO 2002-1719		20020411
PRIORITY APPLN. INFO.:			DE 1999-19949208	A	19991013
			DE 2000-10042696	A	20000831
			US 1999-160547P	P	19991020
			WO 2000-EP9867	W	20001009

OTHER SOURCE(S): MARPAT 134:311105

GI



I

AB The invention relates to the preparation of substituted (Z)-aminomethyleneindolines I [wherein X = O or S; R1 = H, C1-4 alkoxycarbonyl, C2-4 alkanoyl; R2 = HO2C, C1-6 alkoxycarbonyl, C4-7 cycloalkoxycarbonyl, aryloxycarbonyl, aminocarbonyl, or alkyl-substituted aminocarbonyl; R3 = H, C1-6 alkyl, C3-7 cycloalkyl, CF3, heteroaryl, or (un)substituted Ph or naphthyl; R4 and R5 = independently C3-7 cycloalkyl, monosubstituted phenyl] isomers and salts thereof as receptor tyrosine kinase and cyclin/CDK complex inhibitors for the treatment of endothelial cells and tumor cell proliferation. For example, 1-acetyl-6-ethoxycarbonyl-3-(ethoxyphenylmethylene)-2-indolinone and N-(4-aminophenyl)-N-(3-dimethylaminopropyl)acetamide were stirred together in DMF at 100° for 3h followed by addition of piperidine to give I (X = O; R1 = H; R2 = EtO2C; R3 = EtO; R4 = (Me2NCH2CH2CH2)N(Ac)C6H4; R5 = H). I inhibited the proliferation of endothelial cells with an IC50 of 0.003 μM.

IT **334949-31-4P**

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9937034	A1	19991025	AU 1999-37034		19990330 <--
PRIORITY APPLN. INFO.:			DE 1998-19815020	A	19980403
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OTHER SOURCE(S): MARPAT 131:271809
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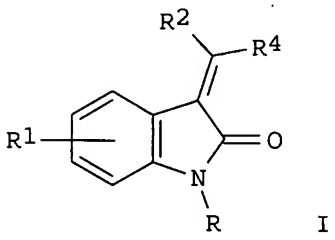


I

AB Title compds. [I; R = H; R1 = H, halo, NO2, (alkanoyl)amino, etc.; R2 = (un)substituted Ph; R4 = NHR3; R3 = heteroannelated Ph, heteroarylalk(en)ylphenyl, etc.] were prepared Thus,2-indolinone was N-acetylated and the product condensed with PhC(OEt)3 to give I (R1 = H, R2 = Ph)(II; R = Ac, R4 = OEt) which was condensed with 5-aminoindole to give II (R = H, R4 = 5-indolylamino). Data for biol. activity of I were given.

=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:283925 CAPLUS
DOCUMENT NUMBER: 134:311105
TITLE: Preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation
INVENTOR(S): Heckel, Armin; Roth, Gerald Juergen; Walter, Rainer; Van Meel, Jacobus; Redemann, Norbert; Tontsch-Grunt, Ulrike; Spevak, Walter; Hilberg, Frank
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 282 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

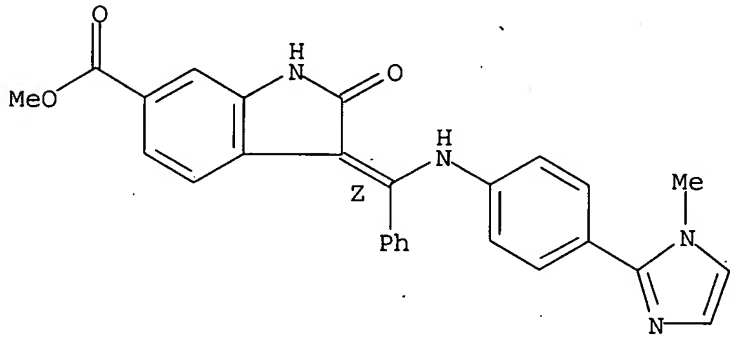
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(title compds.; preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation)

RN 334949-31-4 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-2-oxo-, methyl ester, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **334949-72-3P 334950-27-5P 334950-34-4P**
334950-35-5P 334951-02-9P 334951-03-0P
334951-04-1P 334951-11-0P 334951-73-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(title compds.; preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation)

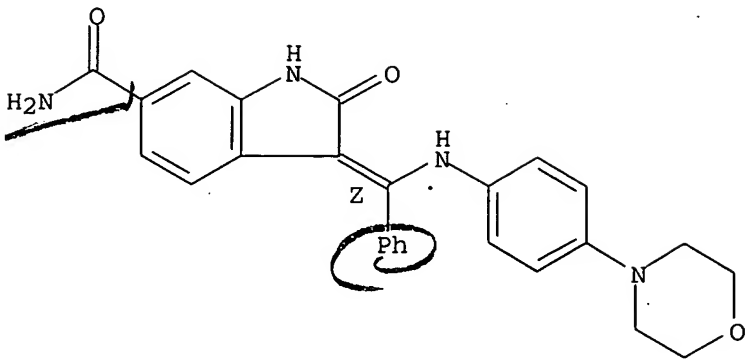
RN 334949-72-3 CAPLUS

CN 1H-Indole-6-carboxamide, 2,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]phenylmethylene]-2-oxo-, (3Z)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

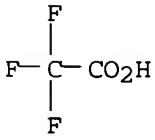
CRN 334949-71-2
CMF C26 H24 N4 O3

Double bond geometry as shown.



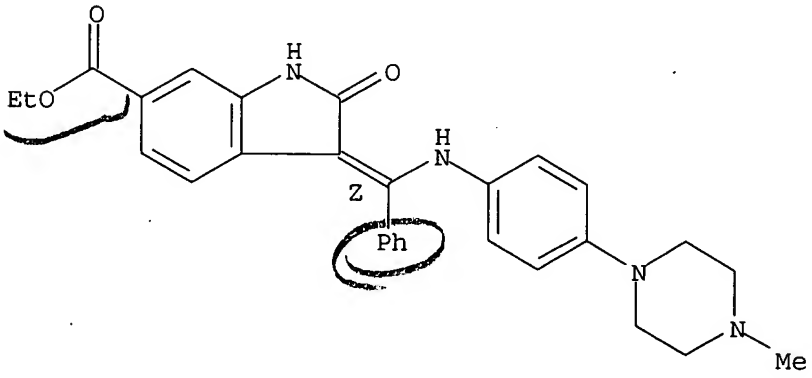
CM 2

CRN 76-05-1
CMF C2 H F3 O2



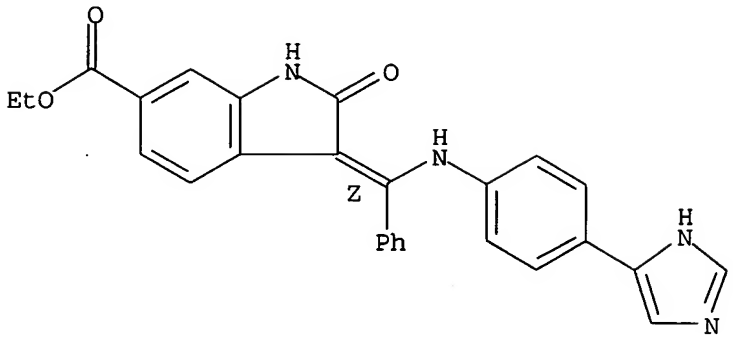
RN 334950-27-5 CAPLUS
CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(4-methyl-1-piperazinyl)phenyl]amino]phenylmethylene]-2-oxo-, ethyl ester, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



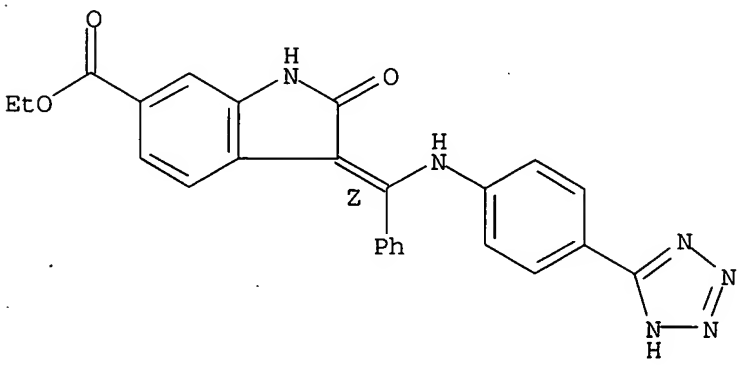
RN 334950-34-4 CAPLUS
CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-2-oxo-, ethyl ester, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



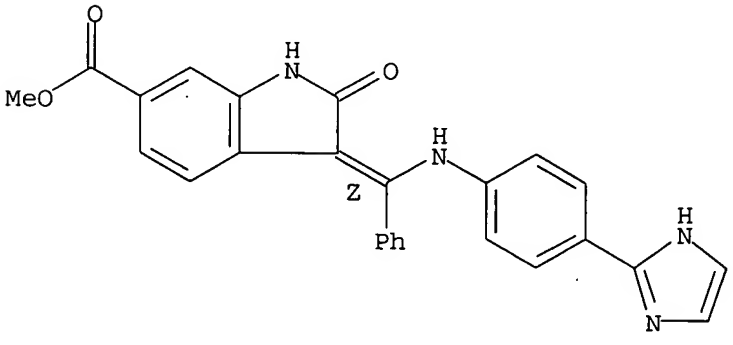
RN 334950-35-5 CAPLUS
CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[phenyl[[4-(1H-tetrazol-5-yl)phenyl]amino]methylene]-, ethyl ester, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 334951-02-9 CAPLUS
CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-2-oxo-, methyl ester, (3Z)- (9CI) (CA INDEX NAME)

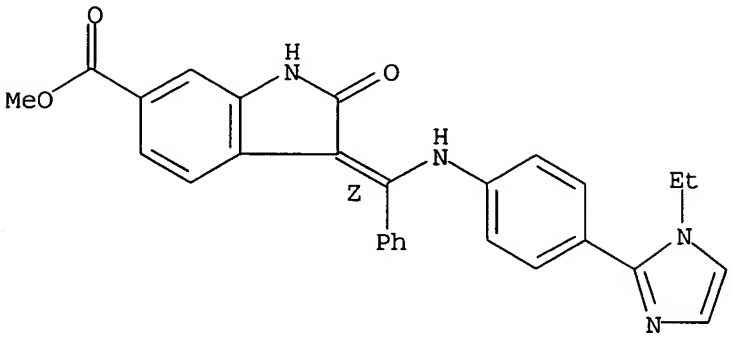
Double bond geometry as shown.



RN 334951-03-0 CAPLUS
CN 1H-Indole-6-carboxylic acid, 3-[[[4-(1-ethyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-2,3-dihydro-2-oxo-, methyl ester, (3Z)-

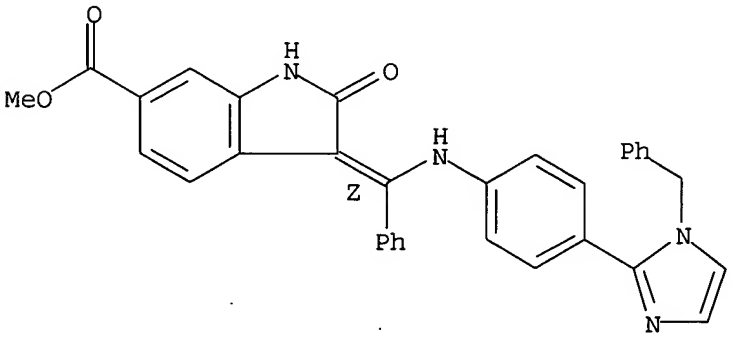
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



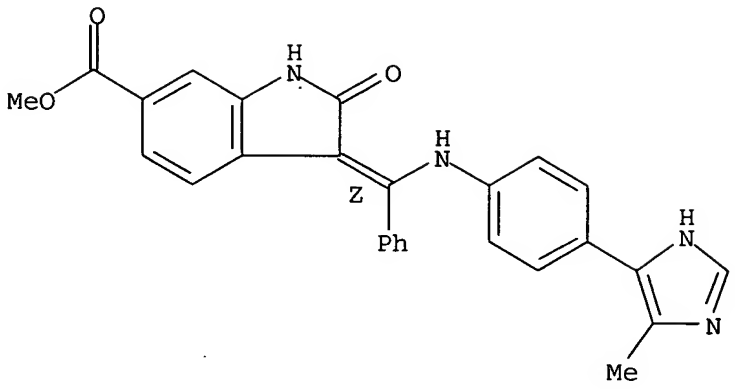
RN 334951-04-1 CAPLUS
CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[phenyl[[4-[1-(phenylmethyl)-1H-imidazol-2-yl]phenyl]amino]methylene]-, methyl ester, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



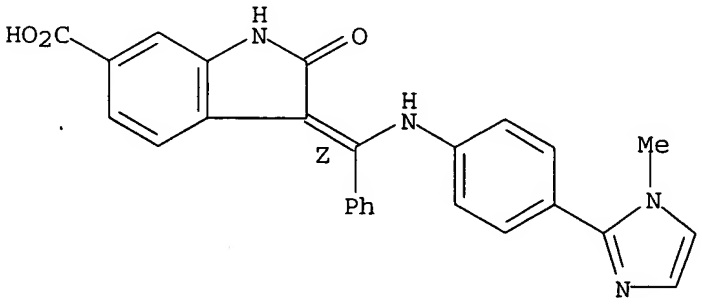
RN 334951-11-0 CAPLUS
CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(5-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-2-oxo-, methyl ester, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 334951-73-4 CAPLUS
CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:688216 CAPLUS
DOCUMENT NUMBER: 133:266726
TITLE: Preparation of 3-(anilinomethylene)oxindoles and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors
INVENTOR(S): Glennon, Kimberley Caroline; Kuyper, Lee Frederick; Lackey, Karen Elizabeth; McNutt, Robert Walton, Jr.
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056710	A1	20000928	WO 2000-US5057	20000228 <--

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MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1165514	A1	20020102	EP 2000-913643	20000228
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JP 2002540097	T2	20021126	JP 2000-606572	20000228
US 6498176	B1	20021224	US 2001-914063	20010822
US 2002099071	A1	20020725	US 2001-966318	20010927
US 6818632	B2	20041116		
US 2004191210	A1	20040930	US 2003-742435	20031219
PRIORITY APPLN. INFO.:			GB 1999-4933 A	19990304
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			WO 2000-US5057 W	20000228
			US 2001-966318 A3	20010927

OTHER SOURCE(S): MARPAT 133:266726

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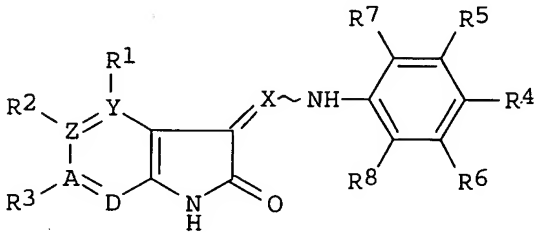

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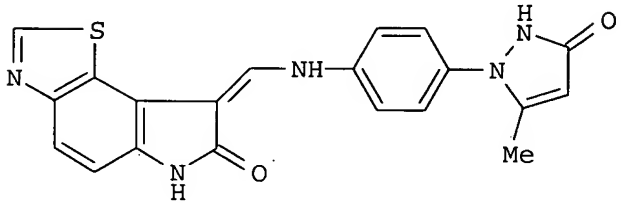


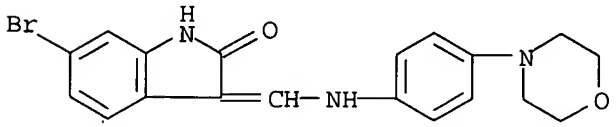
II

AB The title compds. (I) [wherein X = N, CH, CCF3, or C(aliphatic); Y, Z, A, and D = C or N, and the number of N ≤ 1; R1 = H, aliphatic, SH, hydroxy(aliphatic), aryl(aliphatic), cycloalkyl(aliphatic), heterocyclyl(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxycarbonyl, halo, CN, or NO2; R2 = H, aliphatic, hydroxyimino aliphatic, alkoxy(carbonyl), hydroxyaliph., aryl(oxycarbonyl), heterocyclyl, (un)substituted CONH2, NH2, or SO2NH2, halo, OH, NO2, aliphatic sulfonyl, etc.; or R1 and R2 are joined to form an (un)substituted fused heterocyclic ring; R3 = H, aliphatic, hydroxy(aliphatic), (un)substituted NH2, CONH2, or SO2NH2, alkoxy, aryl(oxy), hydroxyaryl, (hydroxy)heterocyclyl, heterocyclyloxy, or halo; or R2 and R3 are joined to form an (un)substituted fused heterocyclic ring; R4 = SO3H, (aliphatic)sulfonyl(aliphatic), (un)substituted SO2NH2, NH2, CONH2, etc.; R5 = H; or R4 and R5 are joined to form an (un)substituted fused heterocyclic ring] were prepared via standard synthetic methods and solution phase library techniques as vascular endothelial growth factor receptor type 2

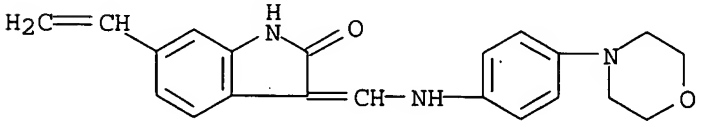
(VEGFR-2), cyclin dependent kinase 2 (CDK2), tyrosine kinase Tie-2 receptor, and colony-stimulating factor 1 receptor kinase (c-fms) inhibitors. For example, a mixture of 8-dimethylaminomethylene-6,8-dihydro-1-thia-3,6-diaza-as-indacene-7-one (preparation given) and 2-(4-aminophenyl)-3-methylpyrazolin-5-one in absolute EtOH was heated with stirring at 90°C for 16 h to give (Z)-II (83%). In substrate phosphorylation assays, II inhibited VEGFR-2 and CDK2 with IC50 values of 1-10 μM and 11-50 μM, resp. I are useful as therapeutic agents in disease states alleviated by the inhibition or antagonism of protein kinase activated signalling pathways in general, and in particular in the pathol. processes which involve aberrant cellular proliferation, such as tumor growth, restenosis, atherosclerosis, and thrombosis. I are particularly useful for suppressing tumor growth by inhibiting tumor-related angiogenesis.

IT **297754-04-2P 297754-40-6P**, 3-[[4-(4-Morpholinyl)anilino]methylidene]-6-vinyl-1,3-dihydro-2H-indol-2-one **297754-49-5P**, 6-Bromo-3-[[4-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)anilino]methylidene]-1,3-dihydro-2H-indol-2-one **297756-72-0P**, 3-[(Z)-[4-(4-Morpholinyl)anilino]methylidene]-6-vinyl-1,3-dihydro-2H-indol-2-one
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of anilinomethylene oxindolones and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors by alkylation and amination of oxindolones via standard or solution phase library methods)

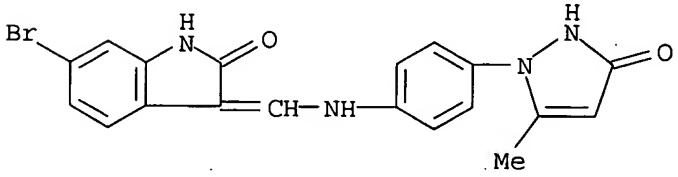
RN 297754-04-2 CAPLUS
CN 2H-Indol-2-one, 6-bromo-1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]methylene]- (9CI) (CA INDEX NAME)



RN 297754-40-6 CAPLUS
CN 2H-Indol-2-one, 6-ethenyl-1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]methylene]- (9CI) (CA INDEX NAME)

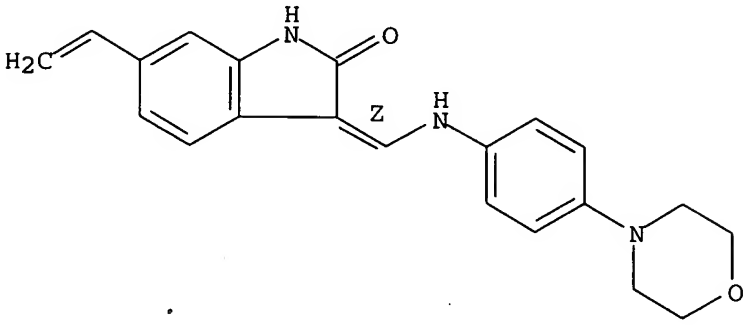


RN 297754-49-5 CAPLUS
CN 2H-Indol-2-one, 6-bromo-3-[[[4-(2,3-dihydro-5-methyl-3-oxo-1H-pyrazol-1-yl)phenyl]amino]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 297756-72-0 CAPLUS
CN 2H-Indol-2-one, 6-ethenyl-1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:227630 CAPLUS
DOCUMENT NUMBER: 132:265083
TITLE: Preparation of 3-aminobenzylideneindolinones as cyclin dependent kinase inhibitors
INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin; Himmelsbach, Frank; Eberlein, Wolfgang; Roth, Gerald; Van Meel, Jacobus C. A.; Redemann, Norbert; Spevak, Walter; Tontsch-Grunt, Ulrike; Von Ruden, Thomas
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 269 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19844003	A1	20000330	DE 1998-19844003	19980925 <--
DE 19937496	A1	20010215	DE 1999-19937496	19990807 <--
CA 2342622	AA	20000406	CA 1999-2342622	19990922 <--
AU 9960863	A1	20000417	AU 1999-60863	19990922 <--
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922 <--
EP 1115704	B1	20030618		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2002525356	T2	20020813	JP 2000-572194		19990922
EE 200100184	A	20020815	EE 2001-184		19990922
AT 243195	E	20030715	AT 1999-947404		19990922
NZ 510845	A	20031031	NZ 1999-510845		19990922
BG 105327	A	20011231	BG 2001-105327		20010309 <--
HR 2001000216	A1	20020430	HR 2001-216		20010321
NO 2001001477	A	20010322	NO 2001-1477		20010322 <--
US 2004058978	A1	20040325	US 2003-666643		20030919
US 6855710	B2	20050215			
PRIORITY APPLN. INFO.:			DE 1998-19844003	A	19980925
			DE 1999-19937496	A	19990807
			WO 1999-EP7040	W	19990922
			US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:265083

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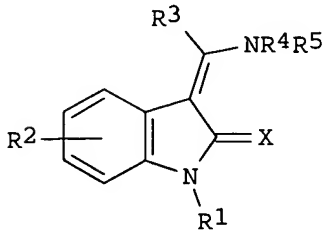


I

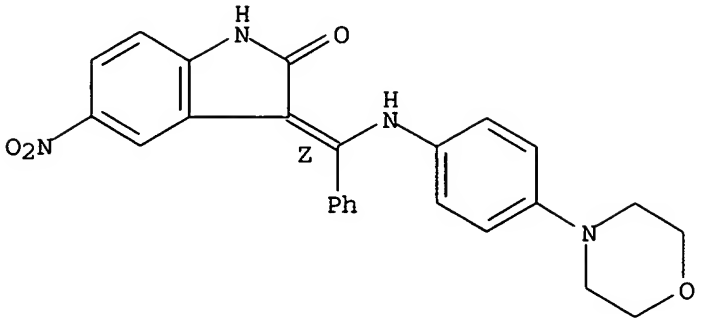
AB Title compds. [I; R1 = H, OH, alkyl; R2 = H, halo, NO2, alkyl; R3 = (un)substituted Ph or -naphthyl; R4 = H or alkyl; R5 = (un)substituted alkylphenyl or -alkylnaphthyl; X = O or S] were prepared Thus, 2-indolinone was N-acetyltated and the product condensed with PhC(OEt)3 to give, after PhNH2 treatment, I (R1 = R2 = R4 = H, R3 = R5 = Ph, X = O). Data for biol. activity of I were given.

IT **262366-61-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-aminobenzylideneindolinones as cyclin dependent kinase inhibitors)

RN 262366-61-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:206644 CAPLUS
DOCUMENT NUMBER: 132:251076
TITLE: Preparation of aminoarylmethylideneindolinones as kinase inhibitors.
INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin; Himmelsbach, Frank; Eberlein, Wolfgang; Van Meel, Jakobus; Redemann, Norbert; Spevak, Walter; Tontsch-Grunt, Ulrike; Von Rueden, Thomas
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 66 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19844003	A1	20000330	DE 1998-19844003	19980925 <--
CA 2342622	AA	20000406	CA 1999-2342622	19990922 <--
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960863	A1	20000417	AU 1999-60863	19990922 <--
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922 <--
EP 1115704	B1	20030618		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100854	T2	20011221	TR 2001-200100854	19990922 <--
JP 2002525356	T2	20020813	JP 2000-572194	19990922
EE 200100184	A	20020815	EE 2001-184	19990922
AT 243195	E	20030715	AT 1999-947404	19990922
NZ 510845	A	20031031	NZ 1999-510845	19990922

PT 1115704	T	20031128	PT 1999-947404	19990922	
ES 2196860	T3	20031216	ES 1999-947404	19990922	
BG 105327	A	20011231	BG 2001-105327	20010309	<--
ZA 2001002260	A	20040419	ZA 2001-2260	20010319	
HR 2001000216	A1	20020430	HR 2001-216	20010321	
NO 2001001477	A	20010322	NO 2001-1477	20010322	<--
US 2004058978	A1	20040325	US 2003-666643	20030919	
US 6855710	B2	20050215			

PRIORITY APPLN. INFO.:

DE 1998-19844003	A	19980925
DE 1999-19937496	A	19990807
WO 1999-EP7040	W	19990922
US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:251076

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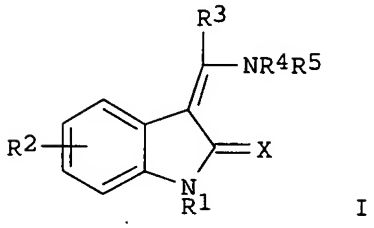


I

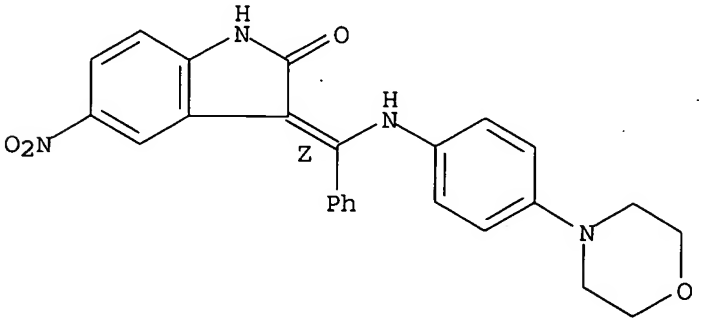
AB Title compds. [I; X = O, S; R1 = H, alkyl; R2 = H, F, Cl, Br, iodo, alkyl, NO2; R3 = (substituted) Ph, naphthyl; R4 = H, alkyl; R5 = (substituted) Ph, naphthyl], were prepared Thus, (Z)-3-[1-(4-piperidinomethylphenylamino)-1-phenylmethylidene]-5-nitro-2-indolinone [prepared from 3-(1-ethoxy-1-phenylmethylidene)-5-nitro-2-indolinone and 4-piperidinomethylaniline in DMF] inhibited proliferation of SCUT 1B tumor proliferation in mice with IC50 = 0.22 μM.

IT **262366-61-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoarylmethylideneindolinones as kinase inhibitors)

RN 262366-61-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



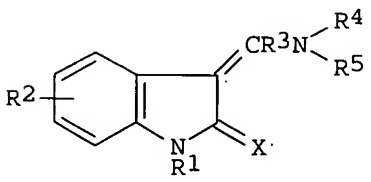
L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:784079 CAPLUS
DOCUMENT NUMBER: 132:12258
TITLE: Aminomethyleneindolinones with antitumor activity
INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Norbert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962882	A1	19991209	WO 1999-EP3692	19990528 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19824922	A1	19991209	DE 1998-19824922	19980604 <--
CA 2328291	AA	19991209	CA 1999-2328291	19990528 <--
AU 9943707	A1	19991220	AU 1999-43707	19990528 <--
AU 764782	B2	20030828		
BR 9910898	A	20010213	BR 1999-10898	19990528 <--
EP 1100779	A1	20010523	EP 1999-926454	19990528 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200003515	T2	20010621	TR 2000-200003515	19990528 <--
EE 200000723	A	20020415	EE 2000-723	19990528
JP 2002516906	T2	20020611	JP 2000-552094	19990528
US 6319918	B1	20011120	US 1999-323499	19990601 <--
ZA 2000005435	A	20020107	ZA 2000-5435	20001005
BG 104938	A	20010629	BG 2000-104938	20001113 <--
NO 2000006138	A	20010201	NO 2000-6138	20001201 <--
HR 2000000831	A1	20011231	HR 2000-831	20001201 <--
US 6545035	B1	20030408	US 2001-969912	20011003

PRIORITY APPLN. INFO.:

DE 1998-19824922	A	19980604
US 1998-92014P	P	19980708
WO 1999-EP3692	W	19990528
US 1999-323499	A3	19990601

OTHER SOURCE(S): MARPAT 132:12258
GI



I

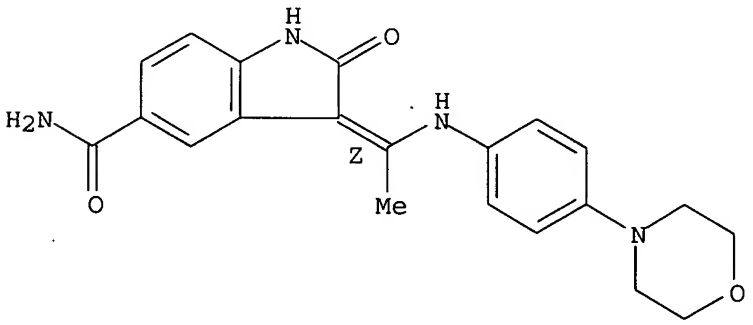
AB Title compds. I [X = O, S; R1 = H, alkoxycarbonyl, alkanoyl; R2 = CO2H, alkoxycarbonyl, (un)substituted CONH2; R3 = H, (un)substituted alkyl; R4 = H, (un)substituted alkyl, Ph, naphthyl, heteroaryl; R5 = H, alkyl] were prepared Thus, 2-oxo-5-indolinecarboxylic acid was attached to Rink resin and treated with tri-Me orthovalerate to give polymer-bound 3-Z-(1-methoxy-1-butylmethylene)-2-oxo-5-indolinecarboxamide which was treated with 4-piperidinomethylaniline to give I [X = O, R1 = 5-CONH2, R2, R4 = h, R3 = Bu, R5 = 4-piperidinomethylanilino]. This compound had an IC50 for inhibition of SKUT-1B cell proliferation of 0.036 μM.

IT **251550-82-0P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminomethyleneindolinones with antitumor activity)

RN 251550-82-0 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-[1-[[4-(4-morpholinyl)phenyl]amino]ethylidene]-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:672749 CAPLUS
DOCUMENT NUMBER: 131:299364
TITLE: Substituted indolinones having an inhibiting effect on kinases and cyclin/CDK complexes
INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Robert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952869	A1	19991021	WO 1999-EP2436	19990410 <--

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,

RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19816624	A1	19991021	DE 1998-19816624	19980415 <--
US 6169106	B1	20010102	US 1999-286983	19990406 <--
CA 2323111	AA	19991021	CA 1999-2323111	19990410 <--
AU 9938149	A1	19991101	AU 1999-38149	19990410 <--
AU 749829	B2	20020704		
BR 9909688	A	20001219	BR 1999-9688	19990410 <--
EP 1071665	A1	20010131	EP 1999-920635	19990410 <--
EP 1071665	B1	20031001		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200002980	T2	20010221	TR 2000-200002980	19990410 <--
EE 200000598	A	20020415	EE 2000-598	19990410
EE 4432	B1	20050215		
JP 2002511449	T2	20020416	JP 2000-543432	19990410
NZ 507967	A	20030429	NZ 1999-507967	19990410
AT 251138	E	20031015	AT 1999-920635	19990410
SK 283824	B6	20040203	SK 2000-1513	19990410
PT 1071665	T	20040227	PT 1999-920635	19990410
ES 2207209	T3	20040516	ES 1999-920635	19990410
TW 510897	B	20021121	TW 1999-88105963	19990414
ZA 2000004623	A	20010307	ZA 2000-4623	20000904 <--
BG 104813	A	20010831	BG 2000-104813	20000929 <--
BG 64443	B1	20050228		
NO 2000005151	A	20001013	NO 2000-5151	20001013 <--

PRIORITY APPLN. INFO.:	DE 1998-19816624	A	19980415
	US 1998-90227P	P	19980622
	WO 1999-EP2436	W	19990410

OTHER SOURCE(S): MARPAT 131:299364

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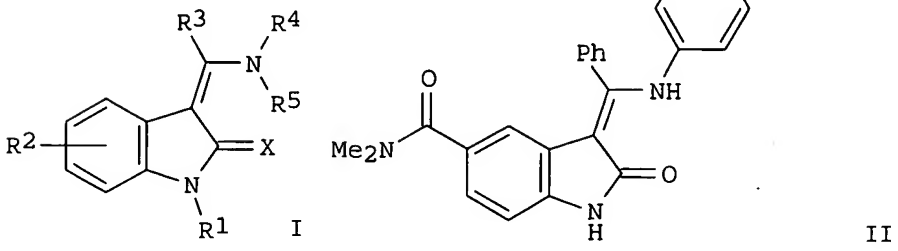


AB The invention relates to substituted indolinones I [X = O or S; R1 = H, alkoxycarbonyl, alkanoyl; R2 = CO2H, alkoxycarbonyl, or (di)(alkyl)aminocarbonyl; R3 = (un)substituted Ph or naphthyl; R4 = H, alkyl; R5 = H, (un)substituted alkyl, cycloalkyl, indanyl, Ph, heteroaryl, pyrrolidinyl, or piperidinyl], their isomers, and their salts, especially their physiol. compatible salts. The compds. have valuable pharmacol. properties, especially an inhibitory effect on various kinases and cyclin/CDK complexes, and on the proliferation of various tumor cells. The invention

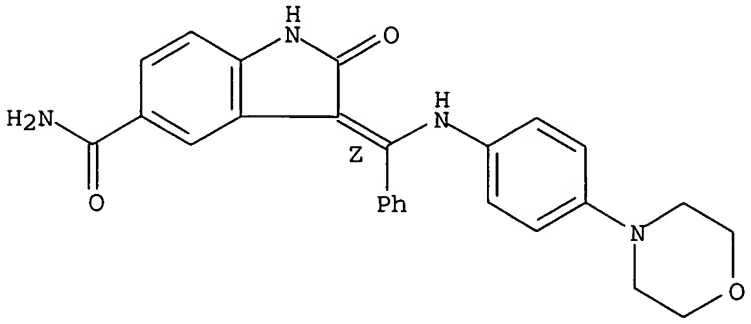
also relates to medicaments containing the compds., to their use, and to methods for producing them. Approx. 160 example compds. and 7 pharmaceutical formulations are described. For instance, title compound II was prepared from 2-indolinone-5-carboxylic acid Me ester in 5 steps: (1) N-acetylation (86%); (2) condensation with PhC(OEt)3 to give the 3-(1-ethoxy-1-phenylmethylene) derivative (67%); (3) condensation of the alkoxymethylene compound with a corresponding amine and deacetylation; (4) saponification of the Me ester; and (5) amidation of the resulting acid with dimethylamine (88%). In an assay against SK-UT-1B lung tumor cells in mice, II had an IC50 value of 0.01 μM.

IT **247083-50-7P 247083-71-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of indolinones as inhibitors of kinases and cyclin/CDK complexes)

RN 247083-50-7 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]phenylmethylene]-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

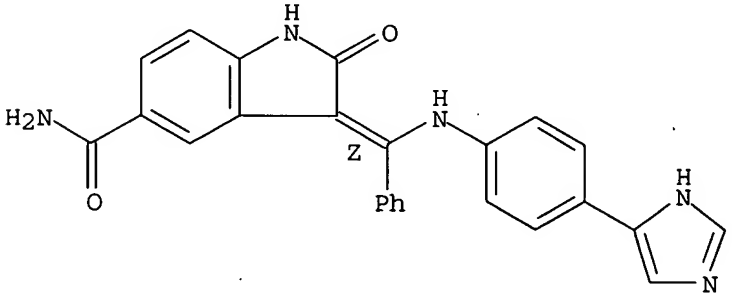
Double bond geometry as shown.



RN 247083-71-2 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:659664 CAPLUS

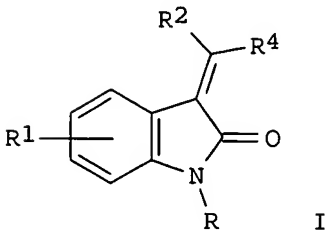
DOCUMENT NUMBER: 131:271809
TITLE: Preparation of 3-(α-heteroarylaminobenzylidene)-2-indolinones as Cyclin dependent kinase inhibitors
INVENTOR(S): Grell, Wolfgang; Walter, Rainer; Heckel, Armin; Himmelsbach, Frank; Wittneben, Helmut; van Meel, Jakobus; Redemann, Norbert; Haigh, Robert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: Ger. Offen., 64 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19815020	A1	19991007	DE 1998-19815020	19980403 <--
US 6043254	A	20000328	US 1999-277063	19990326 <--
WO 9951590	A1	19991014	WO 1999-EP2186	19990330 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937034	A1	19991025	AU 1999-37034	19990330 <--

PRIORITY APPLN. INFO.:

DE 1998-19815020	A	19980403
US 1998-86733P	P	19980526
WO 1999-EP2186	W	19990330

OTHER SOURCE(S): MARPAT 131:271809
GI



I

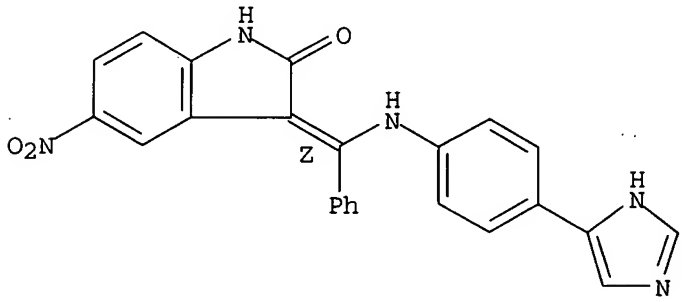
AB Title compds. [I; R = H; R1 = H, halo, NO2, (alkanoyl)amino, etc.; R2 = (un)substituted Ph; R4 = NHR3; R3 = heteroannelated Ph, heteroarylalk(en)ylphenyl, etc.] were prepared Thus,2-indolinone was N-acetylated and the product condensed with PhC(OEt)3 to give I (R1 = H, R2 = Ph)(II; R = Ac, R4 = OEt) which was condensed with 5-aminoindole to give II (R = H, R4 = 5-indolylamino). Data for biol. activity of I were given.

IT **245545-75-9P 245545-89-5P 245545-90-8P 245545-92-0P 245545-95-3P 245546-03-6P 245546-07-0P 245546-19-4P 245546-20-7P**

245546-28-5P 245546-29-6P 245546-32-1P
245546-33-2P 245546-34-3P 245546-35-4P
245546-36-5P 245546-37-6P 245546-39-8P
245546-45-6P 245546-46-7P 245546-47-8P
245546-48-9P 245546-50-3P 245546-57-0P
245546-65-0P 245546-68-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-(α-heteroarylaminobenzylidene)-2-indolinones as cyclin dependent kinase inhibitors)

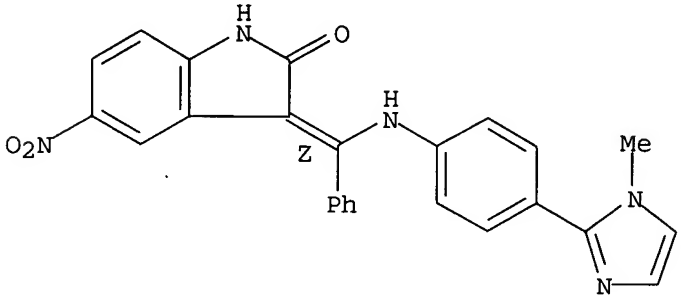
RN 245545-75-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



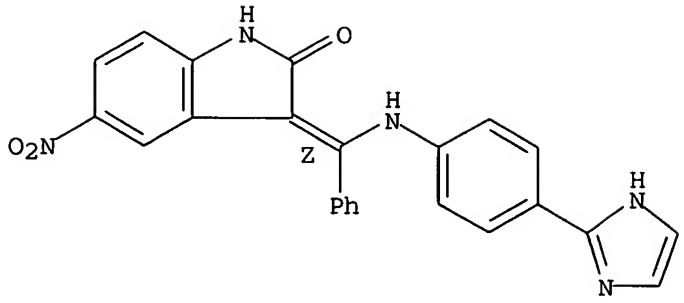
RN 245545-89-5 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



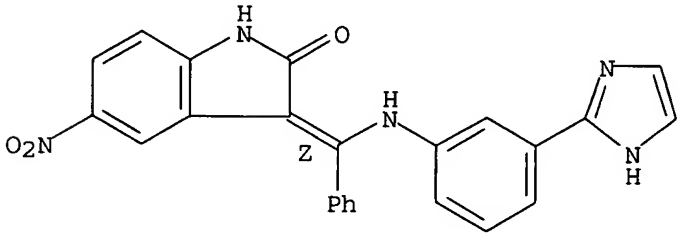
RN 245545-90-8 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



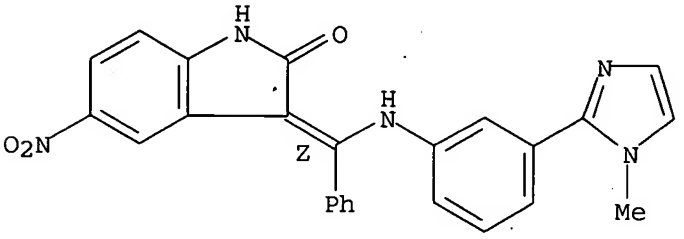
RN 245545-92-0 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[3-(1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



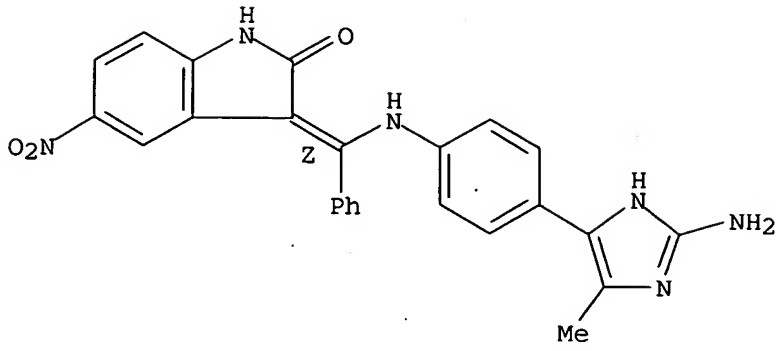
RN 245545-95-3 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[3-(1-methyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



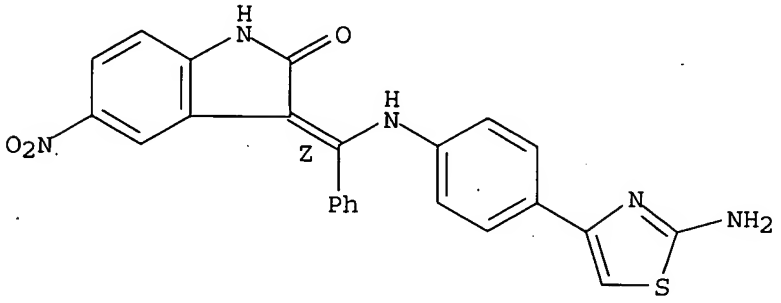
RN 245546-03-6 CAPLUS
CN 2H-Indol-2-one, 3-[[[4-(2-amino-5-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



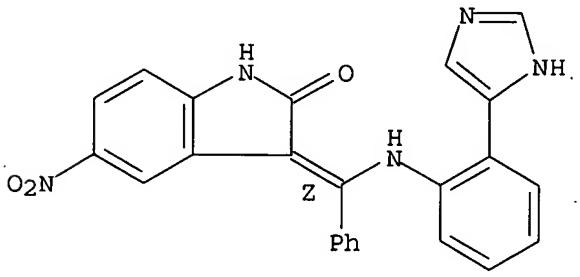
RN 245546-07-0 CAPLUS
CN 2H-Indol-2-one, 3-[[[4-(2-amino-4-thiazolyl)phenyl]amino]phenylmethylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



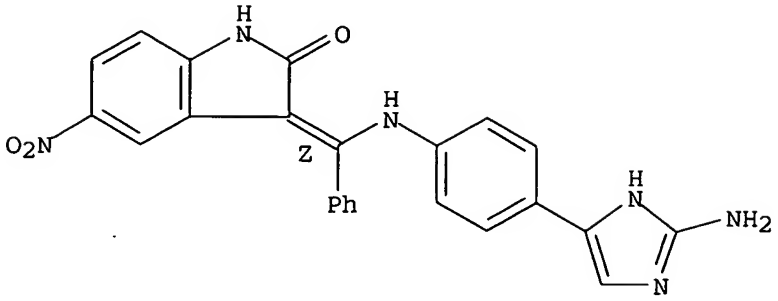
RN 245546-19-4 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[2-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



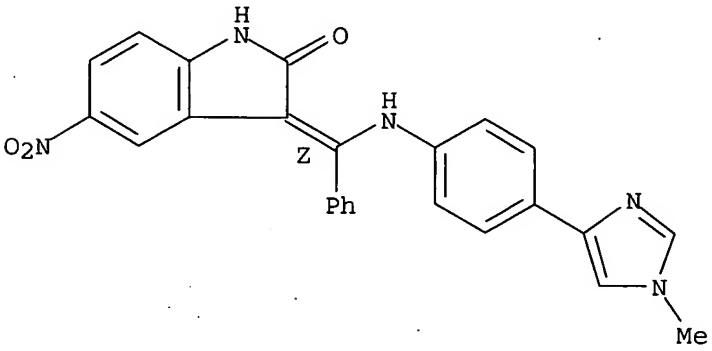
RN 245546-20-7 CAPLUS
CN 2H-Indol-2-one, 3-[[[4-(2-amino-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



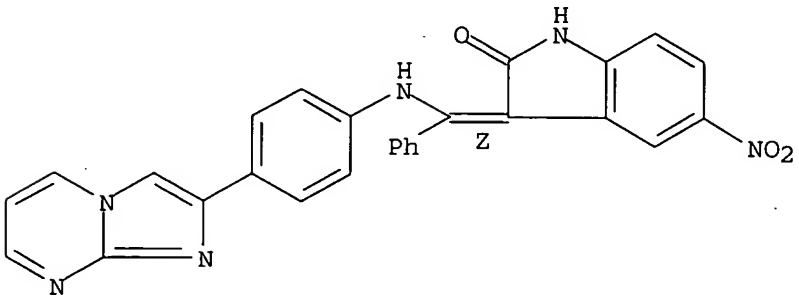
RN 245546-28-5 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



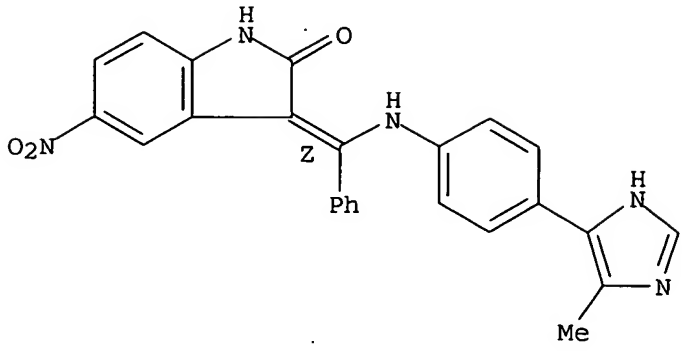
RN 245546-29-6 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[(4-imidazo[1,2-a]pyrimidin-2-ylphenyl)amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



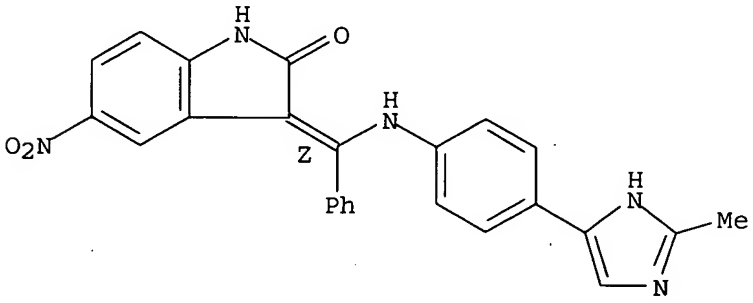
RN 245546-32-1 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(5-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



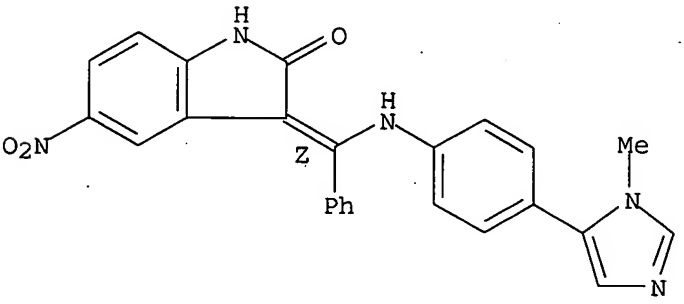
RN 245546-33-2 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(2-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



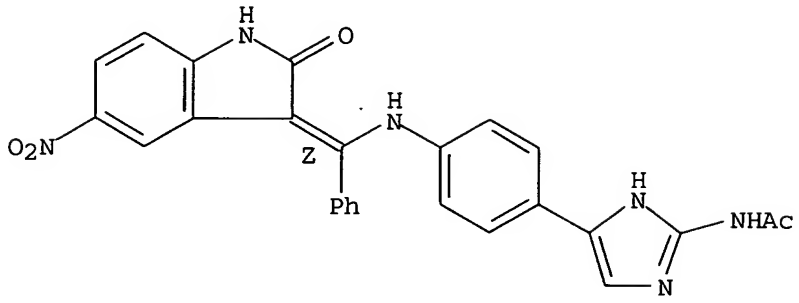
RN 245546-34-3 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-5-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



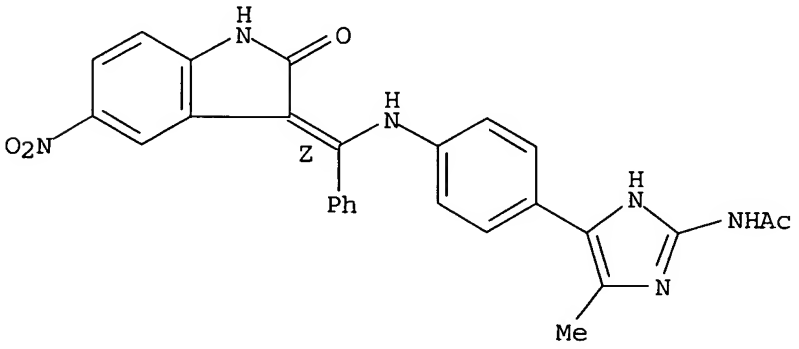
RN 245546-35-4 CAPLUS
CN Acetamide, N-[4-[4-[[(Z)-(1,2-dihydro-5-nitro-2-oxo-3H-indol-3-ylidene)phenylmethyl]amino]phenyl]-1H-imidazol-2-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



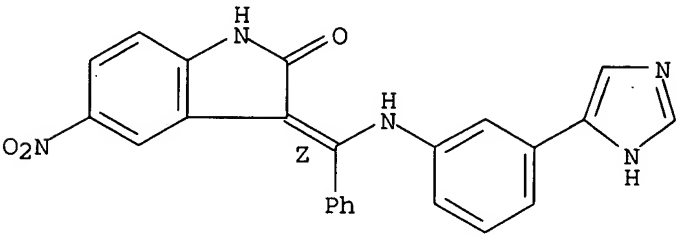
RN 245546-36-5 CAPLUS
CN Acetamide, N-[4-[4-[[(Z)-(1,2-dihydro-5-nitro-2-oxo-3H-indol-3-ylidene)phenylmethyl]amino]phenyl]-5-methyl-1H-imidazol-2-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



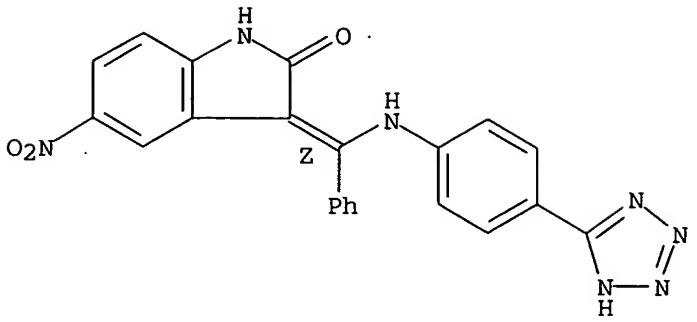
RN 245546-37-6 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[3-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



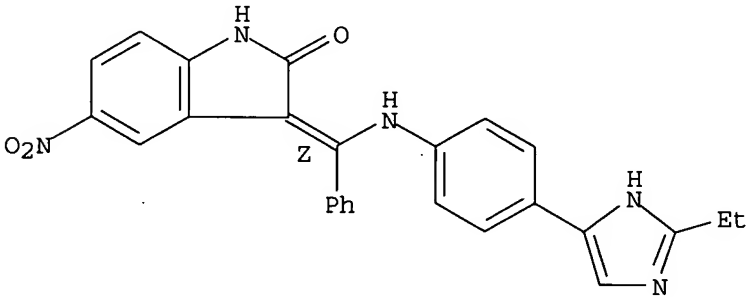
RN 245546-39-8 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-5-nitro-3-[phenyl[[4-(1H-tetrazol-5-yl)phenyl]amino]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



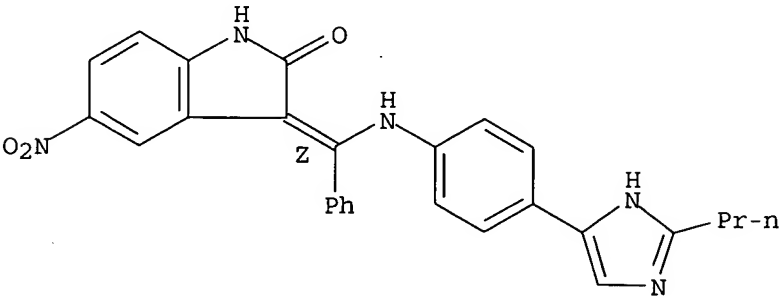
RN 245546-45-6 CAPLUS
CN 2H-Indol-2-one, 3-[[[4-(2-ethyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



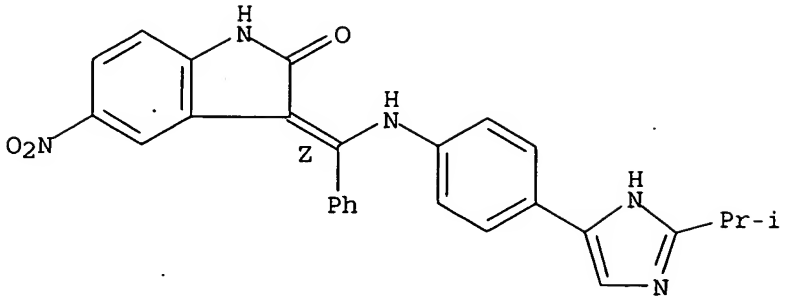
RN 245546-46-7 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-5-nitro-3-[phenyl[[4-(2-propyl-1H-imidazol-4-yl)phenyl]amino]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



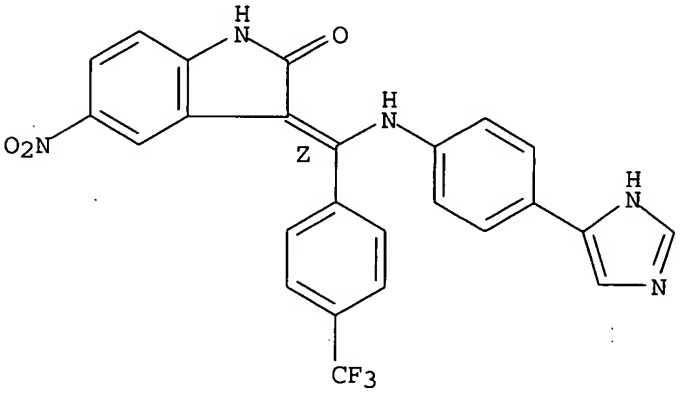
RN 245546-47-8 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-[2-(1-methylethyl)-1H-imidazol-4-yl]phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



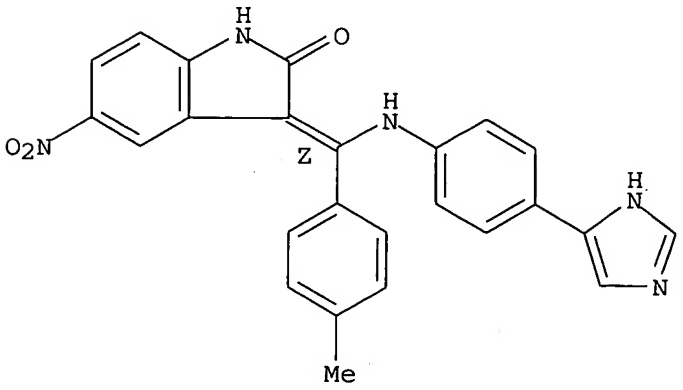
RN 245546-48-9 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino][4-(trifluoromethyl)phenyl]methylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 245546-50-3 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino](4-methylphenyl)methylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

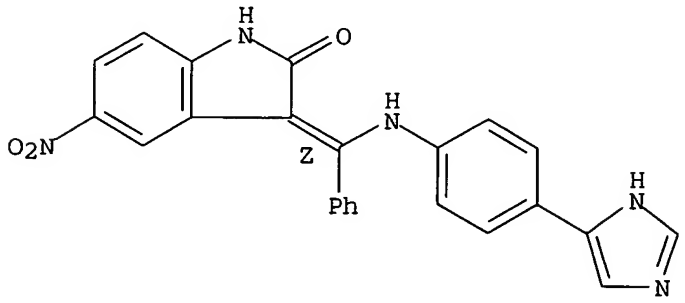
Double bond geometry as shown.



RN 245546-57-0 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-4-

yl)phenyl]amino]phenylmethylene]-5-nitro-, monohydrochloride, (3Z)- (9CI) (CA INDEX NAME)

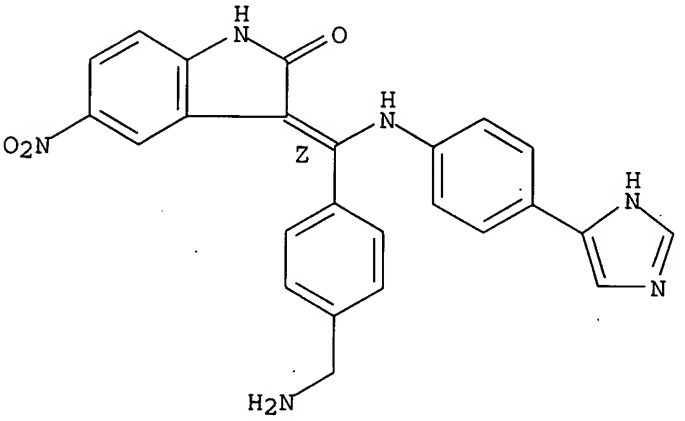
Double bond geometry as shown.



● HCl

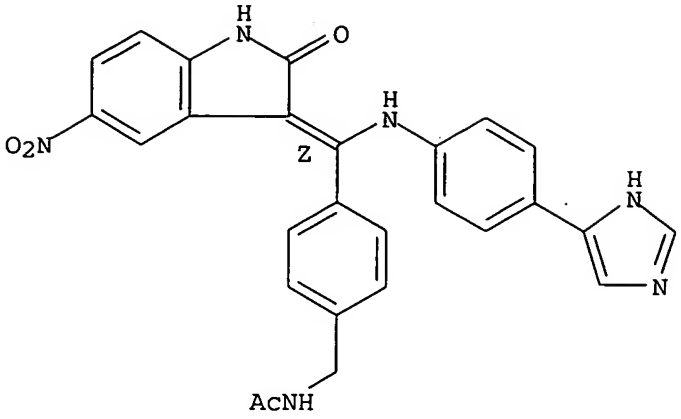
RN 245546-65-0 CAPLUS
CN 2H-Indol-2-one, 3-[[4-(aminomethyl)phenyl][[4-(1H-imidazol-4-yl)phenyl]amino]methylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



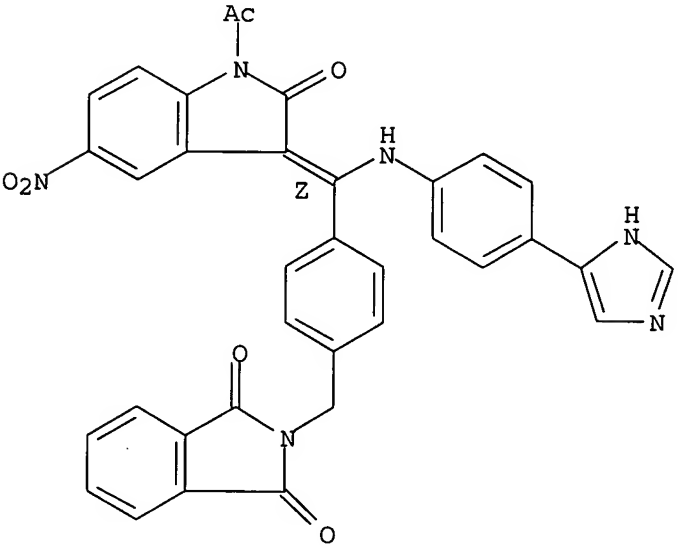
RN 245546-68-3 CAPLUS
CN Acetamide, N-[[4-[(Z)-(1,2-dihydro-5-nitro-2-oxo-3H-indol-3-ylidene)[[4-(1H-imidazol-4-yl)phenyl]amino]methyl]phenyl]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **245547-10-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3-(α-heteroarylaminobenzylidene)-2-indolinones as cyclin dependent kinase inhibitors)
RN 245547-10-8 CAPLUS
CN 2H-Indol-2-one, 1-acetyl-3-[[4-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl][[4-(1H-imidazol-4-yl)phenyl]amino]methylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	93.92	581.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

CA SUBSCRIBER PRICE -20.44 -20.44

STN INTERNATIONAL LOGOFF AT 11:47:48 ON 20 JUN 2005